Dokumentvorlage, Version vom 16.12.2021

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Andexanet alfa (Ondexxya®)

AstraZeneca GmbH

Anhang 4G

Zur Anwendung bei erwachsenen Patienten, die mit einem direkten FXa-Inhibitor (Apixaban oder Rivaroxaban) behandelt werden, wenn aufgrund lebensbedrohlicher oder nicht kontrollierbarer Blutungen eine Aufhebung der Antikoagulation erforderlich ist

Analysen für das Nutzendossier

Stand: 30.06.2025

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Study Disposition
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)
		n (%)	n (%)
Study disposition	Completed	164 (68.0)	169 (72.5)
	Discontinued	77 (32.0)	64 (27.5)
Reason for Discontinuation from Study	Adverse Event	57 (23.7)	49 (21.0)
	Disease Progression	7 (2.9)	9 (3.9)
	Withdrawal By Subject	5 (2.1)	3 (1.3)
	Other	5 (2.1)	2 (0.9)
	Physician Decision	3 (1.2)	1 (0.4)

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.2
Demographics and Baseline Characteristics
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
Age (years)	n (missing)	241 (0)	233 (0)	474 (0)
	Mean (SD)	79.3 (8.44)	78.6 (8.72)	79.0 (8.58)
	Median	81.0	80.0	80.0
	Q1, Q3	75.0, 85.0	74.0, 85.0	74.0, 85.0
	Min, Max	48, 96	42, 96	42, 96
	<65	13 (5.4)	16 (6.9)	29 (6.1)
	65 - 74	45 (18.7)	51 (21.9)	96 (20.3)
	>=75	183 (75.9)	166 (71.2)	349 (73.6)
Sex	n	241	233	474
	Female	111 (46.1)	115 (49.4)	226 (47.7)
	Male	130 (53.9)	118 (50.6)	248 (52.3)
	Missing	0	0	0
Race	n	232	229	461
	Asian	3 (1.3)	4 (1.7)	7 (1.5)
	Black or African American	5 (2.2)	4 (1.7)	9 (2.0)
	Other	7 (3.0)	8 (3.5)	15 (3.3)
	White	217 (93.5)	213 (93.0)	430 (93.3)
	Missing	9	4	13
Ethnicity	n	241	233	474
	Hispanic Or Latino	11 (4.6)	11 (4.7)	22 (4.6)
	Not Hispanic Or Latino	209 (86.7)	205 (88.0)	414 (87.3)
	Not Reported	15 (6.2)	16 (6.9)	31 (6.5)
	Unknown	6 (2.5)	1 (0.4)	7 (1.5)
	Missing	0	0	0
Geographic Region	n	241	233	474
	Europe	212 (88.0)	206 (88.4)	418 (88.2)
	North America	29 (12.0)	27 (11.6)	56 (11.8)
	Missing	0	0	0
Height (cm)	n (missing)	199 (42)	201 (32)	400 (74)
	Mean (SD)	169.97 (9.887)	168.39 (10.471)	169.18 (10.203)
	Median	169.00	169.00	169.00
	Q1, Q3	163.00, 178.00	162.00, 175.00	162.80, 176.00
	Min, Max	148.0, 196.0	129.5, 194.0	129.5, 196.0
Weight (kg)	n (missing)	213 (28)	219 (14)	432 (42)
	Mean (SD)	78.07 (17.779)	74.70 (15.831)	76.37 (16.885)
	Median	78.00	75.00	75.95
	Q1, Q3	66.00, 87.00	62.00, 85.00	64.70, 85.00
	Min, Max	39.0, 179.5	39.8, 120.0	39.0, 179.5

Israel is counted in Europe.
For subjects in the UC arm who receive no treatment by design, their randomization time is used for the calculation.
Baseline Anti-FXa Activity: The participants with enoxaparin as the prior FXa inhibitor are excluded due to their unconvertible unit of anti-FXa activity.
Intended usual care agent: Category 'Not Collected' is for participants enrolled prior to Protocol Amendment 1; 'Prothrombin Complex Concentrate' and 'Other' are for participants enrolled under/after Protocol Amendment 1.

Table 1.2
Demographics and Baseline Characteristics
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
BMI (kg/m^2)	n (missing)	197 (44)	201 (32)	398 (76)
	Mean (SD)	26.82 (5.343)	26.35 (4.677)	26.59 (5.017)
	Median	26.10	25.90	26.00
	Q1, Q3	23.70, 28.70	23.10, 28.90	23.40, 28.90
	Min, Max	16.3, 62.1	15.9, 40.4	15.9, 62.1
	<25	77 (39.1)	86 (42.8)	163 (41.0)
	25-<30	80 (40.6)	76 (37.8)	156 (39.2)
	>=30	40 (20.3)	39 (19.4)	79 (19.8)
Tobacco Use	n	235	227	462
	Current	21 (8.9)	17 (7.5)	38 (8.2)
	Former	71 (30.2)	65 (28.6)	136 (29.4)
	Never	143 (60.9)	145 (63.9)	288 (62.3)
	Missing	6	6	12
Primary Bleeding Location from Core Lab	n	240	232	472
	Intracerebral	215 (89.6)	218 (94.0)	433 (91.7)
	Intraventricular	2 (0.8)	1 (0.4)	3 (0.6)
	Subarachnoid	10 (4.2)	8 (3.4)	18 (3.8)
	Subdural	13 (5.4)	5 (2.2)	18 (3.8)
	Missing	1	1	2
Mechanism of Injury	n	241	233	474
	Spontaneous	211 (87.6)	201 (86.3)	412 (86.9)
	Trauma	30 (12.4)	32 (13.7)	62 (13.1)
	Missing	0	0	0
Average Hematoma Volume of Baseline CT/MRI (mL) from Core Lab	n (missing)	241 (0)	232 (1)	473 (1)
	Mean (SD)	18.77 (22.727)	17.34 (21.808)	18.07 (22.269)
	Median	11.05	9.02	9.90
	Q1, Q3	4.33, 25.36	3.32, 23.31	3.59, 24.50
	Min, Max	0.0, 164.2	0.1, 168.7	0.0, 168.7
	<30 mL	190 (78.8)	193 (83.2)	383 (81.0)
	>=30 mL and <60 mL	36 (14.9)	28 (12.1)	64 (13.5)
	>=60 mL	15 (6.2)	11 (4.7)	26 (5.5)
	<9.90 mL (median)	112 (46.5)	124 (53.4)	236 (49.9)
	>=9.90 mL (median)	129 (53.5)	108 (46.6)	237 (50.1)
ICH Score	n (missing)	241 (0)	233 (0)	474 (0)
	Mean (SD)	1.4 (1.07)	1.3 (1.05)	1.4 (1.06)
	Median	1.0	1.0	1.0
	Q1, Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0
	Min, Max	0, 4	0, 5	0, 5
	< 3	203 (84.2)	204 (87.6)	407 (85.9)
	>= 3	38 (15.8)	29 (12.4)	67 (14.1)

Israel is counted in Europe.
For subjects in the UC arm who receive no treatment by design, their randomization time is used for the calculation.
Baseline Anti-FXa Activity: The participants with enoxaparin as the prior FXa inhibitor are excluded due to their unconvertible unit of anti-FXa activity.
Intended usual care agent: Category 'Not Collected' is for participants enrolled prior to Protocol Amendment 1; 'Prothrombin Complex Concentrate' and 'Other' are for participants enrolled under/after Protocol Amendment 1.

		Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
Participant Presentation Location	n	241	233	474
	Emergency Room/Department	212 (88.0)	216 (92.7)	428 (90.3)
	Inpatient Ward	1 (0.4)	1 (0.4)	2 (0.4)
	Intensive Care Unit	7 (2.9)	4 (1.7)	11 (2.3)
	Other	3 (1.2)	0	3 (0.6)
	Stroke Clinic	12 (5.0)	6 (2.6)	18 (3.8)
	Transfer From Outside Hospital	6 (2.5)	6 (2.6)	12 (2.5)
	Missing	0	0	0
Prior FXa Inhibitor	n	241	233	474
	Apixaban	162 (67.2)	158 (67.8)	320 (67.5)
	Rivaroxaban	79 (32.8)	75 (32.2)	154 (32.5)
	Missing	0	0	0
Indication for Prior FXa Inhibitor	n	241	233	474
	Acute Coronary Syndrome	1 (0.4)	0	1 (0.2)
	Arterial Thromboembolism	6 (2.5)	1 (0.4)	7 (1.5)
	Atrial Fibrillation	206 (85.5)	192 (82.4)	398 (84.0)
	Atrial Flutter	2 (0.8)	2 (0.9)	4 (0.8)
	Chronic Coronary Disease	1 (0.4)	0	1 (0.2)
	Heart Failure	0	1 (0.4)	1 (0.2)
	Other	3 (1.2)	3 (1.3)	6 (1.3)
	Peripheral Arterial Disease	1 (0.4)	1 (0.4)	2 (0.4)
	Prosthetic Valve	1 (0.4)	2 (0.9)	3 (0.6)
	Venous Thromboembolism Prevention	12 (5.0)	15 (6.4)	27 (5.7)
	Venous Thromboembolism Treatment	8 (3.3)	16 (6.9)	24 (5.1)
	Missing	0	0	0
Baseline Anti-FXa Activity (ng/mL)	n (missing)	226 (15)	213 (20)	439 (35)
	Mean (SD)	142.55 (102.769)	165.61 (124.755)	153.74 (114.419)
	Median	112.55	135.90	125.10
	Q1, Q3	68.60, 189.60	76.00, 220.10	71.60, 205.70
	Min, Max	3.0, 592.8	5.2, 733.3	3.0, 733.3
	<30 ng/mL	15 (6.6)	11 (5.2)	26 (5.9)
	>=30 ng/mL	211 (93.4)	202 (94.8)	413 (94.1)
	<75 ng/mL	67 (29.6)	52 (24.4)	119 (27.1)
	>=75 ng/mL	159 (70.4)	161 (75.6)	320 (72.9)
Baseline Anti-FXa Activity by Prior FXa Inhibitor (ng/mL) - Apixaban	n (missing)	152 (89)	147 (86)	299 (175)
	Mean (SD)	124.34 (90.492)	138.02 (95.934)	131.06 (93.302)
	Median	103.85	121.00	110.80
	Q1, Q3	64.45, 162.50	69.30, 183.10	65.90, 168.90
	Min, Max	4.0, 592.8	12.4, 519.7	4.0, 592.8

Israel is counted in Europe.
For subjects in the UC arm who receive no treatment by design, their randomization time is used for the calculation.
Baseline Anti-FXa Activity: The participants with enoxaparin as the prior FXa inhibitor are excluded due to their unconvertible unit of anti-FXa activity.
Intended usual care agent: Category 'Not Collected' is for participants enrolled prior to Protocol Amendment 1; 'Prothrombin Complex Concentrate' and 'Other' are for participants enrolled under/after Protocol Amendment 1.

Table 1.2
Demographics and Baseline Characteristics
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
Baseline Anti-FXa Activity by Prior FXa Inhibitor (ng/mL) - Rivaroxaban	n (missing)	74 (167)	66 (167)	140 (334)
	Mean (SD)	179.96 (116.208)	227.08 (156.625)	202.17 (138.278)
	Median	161.95	192.75	177.95
	Q1, Q3	75.30, 266.40	97.50, 330.60	84.20, 289.00
	Min, Max	3.0, 498.6	5.2, 733.3	3.0, 733.3
Intended Usual Care Agent	n	241	233	474
	Not Collected	63 (26.1)	66 (28.3)	129 (27.2)
	Other	18 (7.5)	11 (4.7)	29 (6.1)
	Prothrombin Complex Concentrate	160 (66.4)	156 (67.0)	316 (66.7)
	Missing	0	0	0
Time From Symptom Onset to Baseline Imaging Scan (minutes)	n (missing)	241 (0)	233 (0)	474 (0)
	Mean (SD)	174.20 (124.251)	176.03 (122.393)	175.10 (123.214)
	Median	134.00	151.00	142.00
	Q1, Q3	79.00, 230.00	86.00, 232.00	84.00, 232.00
	Min, Max	11.0, 683.0	16.0, 715.0	11.0, 715.0
	<180 min	150 (62.2)	143 (61.4)	293 (61.8)
	>=180 min	91 (37.8)	90 (38.6)	181 (38.2)
Time Since Last FXa Inhibitor Dose to Baseline Scan for Bleeding	n	234	233	467
	<180 minutes	22 (9.4)	19 (8.2)	41 (8.8)
	>=180 minutes	212 (90.6)	214 (91.8)	426 (91.2)
	Missing	7	0	7
Time From Symptom Onset to Treatment (hours)	n (missing)	238 (3)	233 (0)	471 (3)
	Mean (SD)	4.44 (2.021)	4.62 (2.120)	4.53 (2.070)
	Median	3.94	4.23	4.07
	Q1, Q3	2.87, 5.58	3.27, 5.50	3.03, 5.58
	Min, Max	1.3, 12.6	1.2, 13.5	1.2, 13.5
Time From Hospitalization to Treatment (hours)	n (missing)	236 (5)	233 (0)	469 (5)
	Mean (SD)	2.44 (1.349)	2.55 (1.322)	2.49 (1.335)
	Median	2.08	2.33	2.20
	Q1, Q3	1.54, 2.88	1.75, 3.08	1.63, 3.00
	Min, Max	0.7, 10.9	0.3, 11.9	0.3, 11.9
Time From the Last FXa Inhibitor Dose to Treatment (hours)	n (missing)	232 (9)	233 (0)	465 (9)
	Mean (SD)	10.01 (4.711)	10.12 (4.507)	10.06 (4.605)
	Median	9.44	9.67	9.55
	Q1, Q3	6.45, 13.20	6.22, 13.83	6.25, 13.60
	Min, Max	2.5, 32.1	3.0, 29.9	2.5, 32.1
	<8 hours	91 (39.2)	94 (40.3)	185 (39.8)
	>=8 hours	141 (60.8)	139 (59.7)	280 (60.2)

Israel is counted in Europe.
For subjects in the UC arm who receive no treatment by design, their randomization time is used for the calculation.
Baseline Anti-FXa Activity: The participants with enoxaparin as the prior FXa inhibitor are excluded due to their unconvertible unit of anti-FXa activity.
Intended usual care agent: Category 'Not Collected' is for participants enrolled prior to Protocol Amendment 1; 'Prothrombin Complex Concentrate' and 'Other' are for participants enrolled under/after Protocol Amendment 1.

Table 1.2
Demographics and Baseline Characteristics
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
Time From Baseline Imaging Scan to Treatment (hours)	n (missing)	238 (3)	233 (0)	471 (3)
	Mean (SD)	1.55 (0.640)	1.69 (0.748)	1.62 (0.699)
	Median	1.47	1.63	1.55
	Q1, Q3	1.08, 1.92	1.13, 2.17	1.12, 2.03
	Min, Max	0.2, 4.5	0.2, 4.2	0.2, 4.5
Systolic Blood Pressure (mmHg)	n (missing)	241 (0)	232 (1)	473 (1)
	Mean (SD)	161.13 (26.424)	157.70 (27.261)	159.45 (26.864)
	Median	162.00	156.00	159.00
	Q1, Q3	143.00, 178.00	139.50, 174.50	141.00, 176.00
	Min, Max	92.0, 252.0	95.0, 259.0	92.0, 259.0
Diastolic Blood Pressure (mmHg)	n (missing)	240 (1)	232 (1)	472 (2)
	Mean (SD)	86.00 (18.412)	84.50 (18.641)	85.26 (18.520)
	Median	84.00	83.00	84.00
	Q1, Q3	74.00, 96.50	73.00, 95.00	73.00, 96.00
	Min, Max	47.0, 149.0	41.0, 154.0	41.0, 154.0
German study center	n	80	83	163

Israel is counted in Europe.
For subjects in the UC arm who receive no treatment by design, their randomization time is used for the calculation.
Baseline Anti-FXa Activity: The participants with enoxaparin as the prior FXa inhibitor are excluded due to their unconvertible unit of anti-FXa activity.
Intended usual care agent: Category 'Not Collected' is for participants enrolled prior to Protocol Amendment 1; 'Prothrombin Complex Concentrate' and 'Other' are for participants enrolled under/after Protocol Amendment 1.

Table 1.3
Concomitant Medication
Safety Analysis Set

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Any Concomitant Medication	239 (100.0)	232 (100.0)	471 (100.0)
ACE INHIBITORS, COMBINATIONS	2 (0.8)	5 (2.2)	7 (1.5)
Co-Perineva	0	1 (0.4)	1 (0.2)
Coveram	1 (0.4)	0	1 (0.2)
Delix Plus	0	1 (0.4)	1 (0.2)
Enalapril And Hydrochlorothiazide (20/12.5 Mg)	0	1 (0.4)	1 (0.2)
Lisam	0	1 (0.4)	1 (0.2)
Lisinopril/Hct	1 (0.4)	0	1 (0.2)
Triplixam	0	1 (0.4)	1 (0.2)
ACE INHIBITORS, PLAIN	108 (45.2)	106 (45.7)	214 (45.4)
Ramipril	49 (20.5)	48 (20.7)	97 (20.6)
Enalapril	19 (7.9)	19 (8.2)	38 (8.1)
Perindopril	13 (5.4)	13 (5.6)	26 (5.5)
Lisinopril	10 (4.2)	14 (6.0)	24 (5.1)
Captopril	11 (4.6)	6 (2.6)	17 (3.6)
Tritace	4 (1.7)	0	4 (0.8)
Coversyl	2 (0.8)	1 (0.4)	3 (0.6)
Delix	1 (0.4)	1 (0.4)	2 (0.4)
Enalaprile	1 (0.4)	1 (0.4)	2 (0.4)
Lisinoprilum	2 (0.8)	0	2 (0.4)
Perindopril-Arginine	0	2 (0.9)	2 (0.4)
Rampiril	2 (0.8)	0	2 (0.4)
(Coversum) Perindopril	1 (0.4)	0	1 (0.2)
Benazapril	0	1 (0.4)	1 (0.2)
Benazepril	0	1 (0.4)	1 (0.2)
Covercyl	0	1 (0.4)	1 (0.2)
Enahexal	1 (0.4)	0	1 (0.2)
Enaladex	0	1 (0.4)	1 (0.2)
Enalaparil	0	1 (0.4)	1 (0.2)
Enalapiril	1 (0.4)	0	1 (0.2)
Enalaprilat	0	1 (0.4)	1 (0.2)
Fositens	1 (0.4)	0	1 (0.2)
Perindopril 2mg, Tablet	1 (0.4)	0	1 (0.2)
Perindopril 4mg, Tablet	1 (0.4)	0	1 (0.2)
Perindoprol	0	1 (0.4)	1 (0.2)
Prestarium	1 (0.4)	0	1 (0.2)
Pã©rindopril Arginine	0	1 (0.4)	1 (0.2)
Ramipiril	0	1 (0.4)	1 (0.2)
Ramipril 1,25 Mg, Cp	0	1 (0.4)	1 (0.2)
Ramiprile	0	1 (0.4)	1 (0.2)
Rampril	0	1 (0.4)	1 (0.2)
Rmipril	1 (0.4)	0	1 (0.2)
Tritace (Ramipril)	0	1 (0.4)	1 (0.2)
Tritace - Ramipril	1 (0.4)	0	1 (0.2)
Tritace Tab	0	1 (0.4)	1 (0.2)
Tritace/Ramipril	1 (0.4)	0	1 (0.2)
ADRENERGICS FOR SYSTEMIC USE	6 (2.5)	4 (1.7)	10 (2.1)
Terbutalin	0	2 (0.9)	2 (0.4)
Bricanyl	1 (0.4)	0	1 (0.2)
Brycanyl	0	1 (0.4)	1 (0.2)
Ipatropium/Salbutamol	1 (0.4)	0	1 (0.2)

Concomitant medications are defined as medications that are started on or after the start of study treatment, or are ongoing at the start of study treatment.
For participants who are randomized into the usual care arm and receive no treatment, their randomization date is used as the start of study treatment.
Medications with partial dates are considered as both prior and concomitant if either type cannot be determined with certainty.
Concomitant medications are coded using WHODrug version Sep2022.
Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Ipratropium Salbutamol	0	1 (0.4)	1 (0.2)
Ipratropium/Salbutamol	1 (0.4)	0	1 (0.2)
Orciprenalin	1 (0.4)	0	1 (0.2)
Reproterol	1 (0.4)	0	1 (0.2)
Salbutamol/Ipratropium	1 (0.4)	0	1 (0.2)
Terbutalin Hemisulfat	0	1 (0.4)	1 (0.2)
Salbutamol/Ipratropium	0	1 (0.4)	1 (0.2)
ADRENERGICS, INHALANTS	45 (18.8)	38 (16.4)	83 (17.6)
Salbutamol	20 (8.4)	19 (8.2)	39 (8.3)
Formoterol	2 (0.8)	3 (1.3)	5 (1.1)
Albuterol	2 (0.8)	2 (0.9)	4 (0.8)
Ipramol	4 (1.7)	0	4 (0.8)
Combivent	3 (1.3)	0	3 (0.6)
Fenoterol	0	2 (0.9)	2 (0.4)
Foster	0	2 (0.9)	2 (0.4)
Olodaterol	2 (0.8)	0	2 (0.4)
Salmeterol	1 (0.4)	1 (0.4)	2 (0.4)
Ventolin	2 (0.8)	0	2 (0.4)
Albuteral	1 (0.4)	0	1 (0.2)
Albuterol Ipratropium	0	1 (0.4)	1 (0.2)
Atrodual	1 (0.4)	0	1 (0.2)
Beclometason/Formoterol (Foster)	0	1 (0.4)	1 (0.2)
Berodualin	0	1 (0.4)	1 (0.2)
Broncovaleas	1 (0.4)	0	1 (0.2)
Budesonide -Formoterol (160/4.5 Ug)	0	1 (0.4)	1 (0.2)
Budesonide-Formoterol	1 (0.4)	0	1 (0.2)
Bufomix Easyhaler	1 (0.4)	0	1 (0.2)
Combiprasal	1 (0.4)	0	1 (0.2)
Duoneb 3ml	0	1 (0.4)	1 (0.2)
Duovent	1 (0.4)	0	1 (0.2)
Epinephrin	0	1 (0.4)	1 (0.2)
Fenoterol + Ipratropium Bromide	1 (0.4)	0	1 (0.2)
Fenoteroli Hydrobormidum + Ipratropii Bromidum	1 (0.4)	0	1 (0.2)
Fluticasone-Vilanterol	0	1 (0.4)	1 (0.2)
Furoate Vilanterol	0	1 (0.4)	1 (0.2)
Indacaterol /Glycopyrronium Bromide(85ug/43mg)	0	1 (0.4)	1 (0.2)
Ipramol Teva / Salbutamol/Ipratropiumbromid	1 (0.4)	0	1 (0.2)
Ipratropium Bromid/ Salbutanol	0	1 (0.4)	1 (0.2)
Ipratropiumbromid/ Salbutanol	0	1 (0.4)	1 (0.2)
Olodaterole/Tiotropium	0	1 (0.4)	1 (0.2)
Relvar Elipta	1 (0.4)	0	1 (0.2)
Salbumatol	1 (0.4)	0	1 (0.2)
Salbutamol Aerosol	0	1 (0.4)	1 (0.2)
Salbutamol Inhalation Liquid	1 (0.4)	0	1 (0.2)
Salbutamol Inhaler	1 (0.4)	0	1 (0.2)
Salbutamol Sulphate	1 (0.4)	0	1 (0.2)
Salbutamol/ Atrovent	0	1 (0.4)	1 (0.2)
Sultamol	1 (0.4)	0	1 (0.2)
Suprarenin	0	1 (0.4)	1 (0.2)
Symbicort	1 (0.4)	0	1 (0.2)
Terbutaline	1 (0.4)	0	1 (0.2)
Teva Combo Sterinebs	0	1 (0.4)	1 (0.2)
Tiotropium/Olaterol	1 (0.4)	0	1 (0.2)
Tiotropium/Olodaterol	1 (0.4)	0	1 (0.2)

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Trimbow	1 (0.4)	0	1 (0.2)
Ultibro	0	1 (0.4)	1 (0.2)
Vilanterol	1 (0.4)	0	1 (0.2)
AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISEASES	1 (0.4)	0	1 (0.2)
Wellvone	1 (0.4)	0	1 (0.2)
AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSURES FOR TOPICAL USE	10 (4.2)	4 (1.7)	14 (3.0)
Diltiazem	3 (1.3)	3 (1.3)	6 (1.3)
Glyceroltrinitrat	2 (0.8)	0	2 (0.4)
Gtn Patch	2 (0.8)	0	2 (0.4)
Beclometason	1 (0.4)	0	1 (0.2)
Diltiazem Additive	1 (0.4)	0	1 (0.2)
Glycerintrinitrat	0	1 (0.4)	1 (0.2)
Glyseroltrinitat	1 (0.4)	0	1 (0.2)
ALKYLATING AGENTS	0	1 (0.4)	1 (0.2)
Pipobroman	0	1 (0.4)	1 (0.2)
ALL OTHER THERAPEUTIC PRODUCTS	10 (4.2)	11 (4.7)	21 (4.5)
Oxygen	2 (0.8)	5 (2.2)	7 (1.5)
Bridion	1 (0.4)	0	1 (0.2)
Calcium Polystyrene Sulfonate	1 (0.4)	0	1 (0.2)
Cholesterol Ointment	1 (0.4)	0	1 (0.2)
Cobicistat	0	1 (0.4)	1 (0.2)
Glykopyrron	1 (0.4)	0	1 (0.2)
Honey Ointment	0	1 (0.4)	1 (0.2)
Kayexalate	1 (0.4)	0	1 (0.2)
Kayexalate 15 G	0	1 (0.4)	1 (0.2)
Oxigen	1 (0.4)	0	1 (0.2)
Oxygen Therapy	0	1 (0.4)	1 (0.2)
Oxygene	0	1 (0.4)	1 (0.2)
Polystyrene Sulfonate	1 (0.4)	0	1 (0.2)
Resonium	1 (0.4)	0	1 (0.2)
Sugammadex	0	1 (0.4)	1 (0.2)
Water	0	1 (0.4)	1 (0.2)
AMINOGLYCOSIDE ANTIBACTERIALS	1 (0.4)	1 (0.4)	2 (0.4)
Amikacine	1 (0.4)	0	1 (0.2)
Gentamycin	0	1 (0.4)	1 (0.2)
AMPHENICOLS	1 (0.4)	1 (0.4)	2 (0.4)
Chloramphenicol	0	1 (0.4)	1 (0.2)
Cloramfenicol	1 (0.4)	0	1 (0.2)
ANESTHETICS, GENERAL	25 (10.5)	31 (13.4)	56 (11.9)
Propofol	19 (7.9)	23 (9.9)	42 (8.9)
Fentanyl	6 (2.5)	15 (6.5)	21 (4.5)
Sufentanil	6 (2.5)	9 (3.9)	15 (3.2)
Remifentanil	3 (1.3)	7 (3.0)	10 (2.1)
Ultiva	3 (1.3)	1 (0.4)	4 (0.8)
Etomidate	2 (0.8)	0	2 (0.4)
Propofol 1%	1 (0.4)	1 (0.4)	2 (0.4)
Sufentanyl	1 (0.4)	1 (0.4)	2 (0.4)
2,6 Diâ€isopropylphenol	1 (0.4)	0	1 (0.2)

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Alfentanil	1 (0.4)	0	1 (0.2)
Diprivan	1 (0.4)	0	1 (0.2)
Diprofol	1 (0.4)	0	1 (0.2)
Disoprivan	1 (0.4)	0	1 (0.2)
Esketamin	0	1 (0.4)	1 (0.2)
Fentanil	0	1 (0.4)	1 (0.2)
Ketamine	0	1 (0.4)	1 (0.2)
Propofol 1% + Lidocain 0.05%	1 (0.4)	0	1 (0.2)
Propofol 2%	0	1 (0.4)	1 (0.2)
Propolipid	1 (0.4)	0	1 (0.2)
Propovol	0	1 (0.4)	1 (0.2)
Remifentamil	1 (0.4)	0	1 (0.2)
Remifentanile	0	1 (0.4)	1 (0.2)
Sulfentanil	0	1 (0.4)	1 (0.2)
Tanyl	1 (0.4)	0	1 (0.2)
ANESTHETICS, LOCAL	8 (3.3)	9 (3.9)	17 (3.6)
Lidocaine	2 (0.8)	4 (1.7)	6 (1.3)
2% Lidocaine	0	1 (0.4)	1 (0.2)
Bupivacaine Adrenaline	0	1 (0.4)	1 (0.2)
Instillagel	1 (0.4)	0	1 (0.2)
Lidocain	1 (0.4)	0	1 (0.2)
Lidocaine 2%	1 (0.4)	0	1 (0.2)
Lidocaine 2% Topical Gel	1 (0.4)	0	1 (0.2)
Lidocaine 4% Patch	0	1 (0.4)	1 (0.2)
Lidocaine With Epinephrine	1 (0.4)	0	1 (0.2)
Lidocaine-Epinephrine	0	1 (0.4)	1 (0.2)
Mepinaest Purum	1 (0.4)	0	1 (0.2)
Ropinaest	1 (0.4)	0	1 (0.2)
Ultracain D-S	0	1 (0.4)	1 (0.2)
Xylocaine	0	1 (0.4)	1 (0.2)
ANTACIDS	5 (2.1)	0	5 (1.1)
Sodium Bicarbonate	3 (1.3)	0	3 (0.6)
Calcium Carbonate	1 (0.4)	0	1 (0.2)
Mablet	1 (0.4)	0	1 (0.2)
ANTI-ACNE PREPARATIONS FOR TOPICAL USE	1 (0.4)	0	1 (0.2)
Chlorhexidine	1 (0.4)	0	1 (0.2)
ANTI-DEMENTIA DRUGS	9 (3.8)	4 (1.7)	13 (2.8)
Donepezil	3 (1.3)	1 (0.4)	4 (0.8)
Memantin	2 (0.8)	1 (0.4)	3 (0.6)
Memantine	1 (0.4)	2 (0.9)	3 (0.6)
Donezipil	0	1 (0.4)	1 (0.2)
Evertas / Rivastigmine	1 (0.4)	0	1 (0.2)
Galantamin	1 (0.4)	0	1 (0.2)
Memantinhydrochlorid	1 (0.4)	0	1 (0.2)
Polmatine / Memantine	1 (0.4)	0	1 (0.2)
Rivastigmin	1 (0.4)	0	1 (0.2)
ANTIADRENERGIC AGENTS, CENTRALLY ACTING	53 (22.2)	51 (22.0)	104 (22.1)
Clonidin	21 (8.8)	22 (9.5)	43 (9.1)
Moxonidin	10 (4.2)	8 (3.4)	18 (3.8)
Clonidine	8 (3.3)	7 (3.0)	15 (3.2)

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Catapresan	5 (2.1)	7 (3.0)	12 (2.5)
Moxonidine	3 (1.3)	3 (1.3)	6 (1.3)
Catapressan	3 (1.3)	1 (0.4)	4 (0.8)
Clonidina	1 (0.4)	3 (1.3)	4 (0.8)
Iterium	2 (0.8)	1 (0.4)	3 (0.6)
Normopresan	2 (0.8)	1 (0.4)	3 (0.6)
Moxonide	0	2 (0.9)	2 (0.4)
Catapressane	0	1 (0.4)	1 (0.2)
Clonidine Hcl	0	1 (0.4)	1 (0.2)
Clonidine Hydrochloride	1 (0.4)	0	1 (0.2)
Hyperium	1 (0.4)	0	1 (0.2)
Methyldopa	0	1 (0.4)	1 (0.2)
Moxonat	1 (0.4)	0	1 (0.2)
Moxonibene	1 (0.4)	0	1 (0.2)
Tenaxum	1 (0.4)	0	1 (0.2)
ANTIADRENERGIC AGENTS, PERIPHERALLY ACTING	112 (46.9)	97 (41.8)	209 (44.4)
Urapidil	76 (31.8)	64 (27.6)	140 (29.7)
Ebrantil	13 (5.4)	12 (5.2)	25 (5.3)
Doxazosin	9 (3.8)	9 (3.9)	18 (3.8)
Doxazosine	4 (1.7)	3 (1.3)	7 (1.5)
Uradipil	1 (0.4)	5 (2.2)	6 (1.3)
Doxazosina	2 (0.8)	3 (1.3)	5 (1.1)
Eupressyl	2 (0.8)	1 (0.4)	3 (0.6)
Cardura	1 (0.4)	1 (0.4)	2 (0.4)
Doxazosin Mesylate	2 (0.8)	0	2 (0.4)
Elgadil	1 (0.4)	1 (0.4)	2 (0.4)
Hypotrit	0	2 (0.9)	2 (0.4)
Urapidile	1 (0.4)	1 (0.4)	2 (0.4)
Cadex	1 (0.4)	0	1 (0.2)
Cadex (Doxazosin Mesylate)	0	1 (0.4)	1 (0.2)
Cadex-Doxazosin	1 (0.4)	0	1 (0.2)
Daxazosin	1 (0.4)	0	1 (0.2)
Doxacor	1 (0.4)	0	1 (0.2)
Doxar (Doxazosin)	0	1 (0.4)	1 (0.2)
Doxasozin	1 (0.4)	0	1 (0.2)
Doxatosin	0	1 (0.4)	1 (0.2)
Doxazocin Meysylate	0	1 (0.4)	1 (0.2)
Doxazosinum	1 (0.4)	0	1 (0.2)
Ebrabtil	0	1 (0.4)	1 (0.2)
Ebranitil	0	1 (0.4)	1 (0.2)
Ebrantil 250 Mg/50ml	0	1 (0.4)	1 (0.2)
Ebrantil Ret.	1 (0.4)	0	1 (0.2)
Ebrantil/ Ubrapidil	0	1 (0.4)	1 (0.2)
Ebrantil/Urapidil	0	1 (0.4)	1 (0.2)
Prazosin	0	1 (0.4)	1 (0.2)
Tachyben	1 (0.4)	0	1 (0.2)
Tachybene	1 (0.4)	0	1 (0.2)
Terazosab	1 (0.4)	0	1 (0.2)
Terazosine	1 (0.4)	0	1 (0.2)
Terrazosab	1 (0.4)	0	1 (0.2)
Uradipilo	1 (0.4)	0	1 (0.2)
Urapedil	0	1 (0.4)	1 (0.2)
Urapidil (50mg/10ml)	1 (0.4)	0	1 (0.2)
Urapidil 100 Mg/50 Ml	0	1 (0.4)	1 (0.2)

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Urapidil 150mg/50ml	0	1 (0.4)	1 (0.2)
Urapidil 50 Mg/10 Ml	0	1 (0.4)	1 (0.2)
Urapidil Clorydrate	1 (0.4)	0	1 (0.2)
Urapidilo	0	1 (0.4)	1 (0.2)
ANTIARRHYTHMICS, CLASS I AND III	33 (13.8)	22 (9.5)	55 (11.7)
Amiodarone	9 (3.8)	9 (3.9)	18 (3.8)
Amiodaron	8 (3.3)	4 (1.7)	12 (2.5)
Cordarone	5 (2.1)	1 (0.4)	6 (1.3)
Propafenone	2 (0.8)	1 (0.4)	3 (0.6)
Amidarone	0	2 (0.9)	2 (0.4)
Amiodorone	1 (0.4)	1 (0.4)	2 (0.4)
Flecainide	2 (0.8)	0	2 (0.4)
Amiadarone	1 (0.4)	0	1 (0.2)
Amiadoron	1 (0.4)	0	1 (0.2)
Amiocard	1 (0.4)	0	1 (0.2)
Amiodarona	0	1 (0.4)	1 (0.2)
Amiodarone Hcl	0	1 (0.4)	1 (0.2)
Amiodarone Hcl Dextrose	0	1 (0.4)	1 (0.2)
Amiodarone Hydrochloride	1 (0.4)	0	1 (0.2)
Amiodoron	1 (0.4)	0	1 (0.2)
Apocard	1 (0.4)	0	1 (0.2)
Cordarex	0	1 (0.4)	1 (0.2)
Flecaine	0	1 (0.4)	1 (0.2)
Flecainid	1 (0.4)	0	1 (0.2)
Procor	0	1 (0.4)	1 (0.2)
Rythmol Tab 150	0	1 (0.4)	1 (0.2)
Tambocor	1 (0.4)	0	1 (0.2)
ANTIBIOTICS FOR TOPICAL USE	1 (0.4)	6 (2.6)	7 (1.5)
Mupirocin	0	3 (1.3)	3 (0.6)
Gentamicina Cream	1 (0.4)	0	1 (0.2)
Mupriocin	0	1 (0.4)	1 (0.2)
Polysporin Cream - Polymyxin B Sulfate And Bacitracin Zinc	0	1 (0.4)	1 (0.2)
Synthomycine	0	1 (0.4)	1 (0.2)
Esketamin	1 (0.4)	0	1 (0.2)
ANTIDEPRESSANTS	59 (24.7)	43 (18.5)	102 (21.7)
Mirtazapin	10 (4.2)	12 (5.2)	22 (4.7)
Escitalopram	3 (1.3)	10 (4.3)	13 (2.8)
Mirtazapine	8 (3.3)	4 (1.7)	12 (2.5)
Trazodone	5 (2.1)	5 (2.2)	10 (2.1)
Sertralin	4 (1.7)	2 (0.9)	6 (1.3)
Sertraline	3 (1.3)	2 (0.9)	5 (1.1)
Citalopram	2 (0.8)	2 (0.9)	4 (0.8)
Fluoxetine	3 (1.3)	0	3 (0.6)
Venlafaxin	2 (0.8)	1 (0.4)	3 (0.6)
Duloxetin	2 (0.8)	0	2 (0.4)
Duloxetine	1 (0.4)	1 (0.4)	2 (0.4)
Mianserine	1 (0.4)	1 (0.4)	2 (0.4)
Sertralina	1 (0.4)	1 (0.4)	2 (0.4)
Venlafaxine	1 (0.4)	1 (0.4)	2 (0.4)
Bupropion	0	1 (0.4)	1 (0.2)
Chlorhydrate De Fluoxã©tine	0	1 (0.4)	1 (0.2)
Ciperalex	1 (0.4)	0	1 (0.2)

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Cipralex	1 (0.4)	0	1 (0.2)
Cymbalta	0	1 (0.4)	1 (0.2)
Cymbalta 60 Mg	1 (0.4)	0	1 (0.2)
Cymbalta/ Duloxetin	0	1 (0.4)	1 (0.2)
Duloxetine 60mg, Capsule	1 (0.4)	0	1 (0.2)
Escitalex	1 (0.4)	0	1 (0.2)
Fluoxetin	1 (0.4)	0	1 (0.2)
Mirtazapine Teva	0	1 (0.4)	1 (0.2)
Mirtazepin	1 (0.4)	0	1 (0.2)
Mirzasna	1 (0.4)	0	1 (0.2)
Nortriptyline	0	1 (0.4)	1 (0.2)
Opipramol	1 (0.4)	0	1 (0.2)
Opipramol Dihdochlorid	1 (0.4)	0	1 (0.2)
Paroxat	0	1 (0.4)	1 (0.2)
Paroxetine_teva Tab 20 Mg	1 (0.4)	0	1 (0.2)
Serenada	1 (0.4)	0	1 (0.2)
Sertraline Hcl	0	1 (0.4)	1 (0.2)
Sipralexa	1 (0.4)	0	1 (0.2)
Trasodone	1 (0.4)	0	1 (0.2)
Trazadone	1 (0.4)	0	1 (0.2)
Trazodil	1 (0.4)	0	1 (0.2)
Trazodon	1 (0.4)	0	1 (0.2)
Trazodon Hydrochlorid	0	1 (0.4)	1 (0.2)
Trazodona	0	1 (0.4)	1 (0.2)
Trazodone Hydrochloride	1 (0.4)	0	1 (0.2)
Trittico	1 (0.4)	0	1 (0.2)
Trittico Ac	1 (0.4)	0	1 (0.2)
Venlafaxina	0	1 (0.4)	1 (0.2)
Venlafaxine Lp 75 Mg	1 (0.4)	0	1 (0.2)
ANTIDIARRHEAL MICROORGANISMS	7 (2.9)	5 (2.2)	12 (2.5)
Antibiophilus	3 (1.3)	0	3 (0.6)
Lactobacillus Rhamnosus	2 (0.8)	0	2 (0.4)
Enterol (Probiotic)	0	1 (0.4)	1 (0.2)
Lactobacillus	0	1 (0.4)	1 (0.2)
Lactobasillus Rhamnosus	1 (0.4)	0	1 (0.2)
Omniflora	0	1 (0.4)	1 (0.2)
Probinul	1 (0.4)	0	1 (0.2)
Ultralevure	0	1 (0.4)	1 (0.2)
Yovis	0	1 (0.4)	1 (0.2)
ANTIEMETICS AND ANTINAUSEANTS	74 (31.0)	72 (31.0)	146 (31.0)
Ondansetron	35 (14.6)	27 (11.6)	62 (13.2)
Metoclopramide	15 (6.3)	20 (8.6)	35 (7.4)
Granisetron	9 (3.8)	6 (2.6)	15 (3.2)
Metoclopramid	7 (2.9)	7 (3.0)	14 (3.0)
Dimenhydrinat	6 (2.5)	4 (1.7)	10 (2.1)
Zofran	4 (1.7)	4 (1.7)	8 (1.7)
Ondasetron	5 (2.1)	2 (0.9)	7 (1.5)
Scopolamine	4 (1.7)	3 (1.3)	7 (1.5)
Dimenhydrinate	3 (1.3)	3 (1.3)	6 (1.3)
Alizapride	0	4 (1.7)	4 (0.8)
Ondansentron	2 (0.8)	1 (0.4)	3 (0.6)
Mcp	1 (0.4)	1 (0.4)	2 (0.4)
Prochlorperazine	0	2 (0.9)	2 (0.4)

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Scopolamin	1 (0.4)	1 (0.4)	2 (0.4)
Vomex	0	2 (0.9)	2 (0.4)
Dehydrobentzperidol	1 (0.4)	0	1 (0.2)
Granisteron	1 (0.4)	0	1 (0.2)
Granistron	0	1 (0.4)	1 (0.2)
Meclizine	0	1 (0.4)	1 (0.2)
Metoclopramid (Mcp)	1 (0.4)	0	1 (0.2)
Metoclopramide Hydrochloride	1 (0.4)	0	1 (0.2)
Odansetron	1 (0.4)	0	1 (0.2)
Ondansan	1 (0.4)	0	1 (0.2)
Ondansedron	0	1 (0.4)	1 (0.2)
Ondansetrone	0	1 (0.4)	1 (0.2)
Paspertin (Metoclopramid Hydrochlorid)	1 (0.4)	0	1 (0.2)
Primperan	0	1 (0.4)	1 (0.2)
Scopoderm Tts	1 (0.4)	0	1 (0.2)
Scopolamine Patch (1mg/3day)	0	1 (0.4)	1 (0.2)
ANTIEPILEPTICS	43 (18.0)	46 (19.8)	89 (18.9)
Levetiracetam	23 (9.6)	33 (14.2)	56 (11.9)
Keppra	6 (2.5)	6 (2.6)	12 (2.5)
Lacosamid	4 (1.7)	2 (0.9)	6 (1.3)
Clobazam	3 (1.3)	1 (0.4)	4 (0.8)
Lamotrigin	1 (0.4)	2 (0.9)	3 (0.6)
Phenytoin	1 (0.4)	2 (0.9)	3 (0.6)
Pregabalin	3 (1.3)	0	3 (0.6)
Rivotril	2 (0.8)	1 (0.4)	3 (0.6)
Diazepam	1 (0.4)	1 (0.4)	2 (0.4)
Kepra	2 (0.8)	0	2 (0.4)
Lacosamide	2 (0.8)	0	2 (0.4)
Valproat	1 (0.4)	1 (0.4)	2 (0.4)
Valproic Acid	1 (0.4)	1 (0.4)	2 (0.4)
Vimpat	2 (0.8)	0	2 (0.4)
Clonex	1 (0.4)	0	1 (0.2)
Depakin	1 (0.4)	0	1 (0.2)
Depalept	1 (0.4)	0	1 (0.2)
Depalept Chrono	1 (0.4)	0	1 (0.2)
Diacepam	1 (0.4)	0	1 (0.2)
Lacosamit	1 (0.4)	0	1 (0.2)
Lamictal	0	1 (0.4)	1 (0.2)
Lancosamid	0	1 (0.4)	1 (0.2)
Levetiracepam	1 (0.4)	0	1 (0.2)
Levetiracetam (Keppra)	1 (0.4)	0	1 (0.2)
Levetiracetam Hcl	0	1 (0.4)	1 (0.2)
Levetirecetam	1 (0.4)	0	1 (0.2)
Leviteracetam	0	1 (0.4)	1 (0.2)
Levitracetam	0	1 (0.4)	1 (0.2)
Levtiracetam	1 (0.4)	0	1 (0.2)
Locasamid	1 (0.4)	0	1 (0.2)
Lyrica	1 (0.4)	0	1 (0.2)
Midazolam	1 (0.4)	0	1 (0.2)
Mysoline	0	1 (0.4)	1 (0.2)
Phenobarbital	0	1 (0.4)	1 (0.2)
Pregabador	1 (0.4)	0	1 (0.2)
Topiramat	1 (0.4)	0	1 (0.2)
Valporic Acid	0	1 (0.4)	1 (0.2)

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Valproic	1 (0.4)	0	1 (0.2)
Valproinsã¤ure	1 (0.4)	0	1 (0.2)
ANTIFIBRINOLYTICS	8 (3.3)	8 (3.4)	16 (3.4)
Tranexamic Acid	6 (2.5)	5 (2.2)	11 (2.3)
Hexakapron	1 (0.4)	1 (0.4)	2 (0.4)
Exacyl	1 (0.4)	0	1 (0.2)
Tranexamic Acide	0	1 (0.4)	1 (0.2)
Tranexaminic Acid	0	1 (0.4)	1 (0.2)
Tranexamsã¤ure	1 (0.4)	0	1 (0.2)
ANTIFUNGALS FOR TOPICAL USE	10 (4.2)	7 (3.0)	17 (3.6)
Nystatin	1 (0.4)	2 (0.9)	3 (0.6)
Daktozin	1 (0.4)	1 (0.4)	2 (0.4)
Betamethazone Clotrimazole	0	1 (0.4)	1 (0.2)
Candido-Hermal Soft	1 (0.4)	0	1 (0.2)
Candio Hermal	1 (0.4)	0	1 (0.2)
Canesten	1 (0.4)	0	1 (0.2)
Canifug	0	1 (0.4)	1 (0.2)
Clotrimaderm	1 (0.4)	0	1 (0.2)
Clotrimazole, Hydrocortisone Acetate	1 (0.4)	0	1 (0.2)
Econazole	1 (0.4)	0	1 (0.2)
Econazole 1%	1 (0.4)	0	1 (0.2)
Gentian Violet	0	1 (0.4)	1 (0.2)
Hydroagisten Cream	1 (0.4)	0	1 (0.2)
Ketoconazole 2%	1 (0.4)	0	1 (0.2)
Lamisil Cream	0	1 (0.4)	1 (0.2)
Miconazole	0	1 (0.4)	1 (0.2)
Nizoral	1 (0.4)	0	1 (0.2)
Travocort	1 (0.4)	0	1 (0.2)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	15 (6.3)	9 (3.9)	24 (5.1)
Lumigan	2 (0.8)	1 (0.4)	3 (0.6)
Bimatoprost	1 (0.4)	1 (0.4)	2 (0.4)
Combigan	2 (0.8)	0	2 (0.4)
Dorzolamid	2 (0.8)	0	2 (0.4)
Latanoprost	0	2 (0.9)	2 (0.4)
Travoprost	1 (0.4)	1 (0.4)	2 (0.4)
Trusopt	2 (0.8)	0	2 (0.4)
Azarga	0	1 (0.4)	1 (0.2)
Azopt	1 (0.4)	0	1 (0.2)
Brimodimin	1 (0.4)	0	1 (0.2)
Brimonidin	0	1 (0.4)	1 (0.2)
Brinzolamid	0	1 (0.4)	1 (0.2)
Brinzolamid Eye Drops	0	1 (0.4)	1 (0.2)
Clonidin Eye Drops	0	1 (0.4)	1 (0.2)
Cos Duo (Eye Drop)	0	1 (0.4)	1 (0.2)
Cosopt	0	1 (0.4)	1 (0.2)
Dorzolamide	1 (0.4)	0	1 (0.2)
Lalanomel	1 (0.4)	0	1 (0.2)
Latanoprost Eye Drops	0	1 (0.4)	1 (0.2)
Latanoprost Eye Drops Solution	1 (0.4)	0	1 (0.2)
Latanotim Vision	1 (0.4)	0	1 (0.2)
Monoprost	0	1 (0.4)	1 (0.2)
Tafluprost	1 (0.4)	0	1 (0.2)

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Tavoprost	1 (0.4)	0	1 (0.2)
Timolol	1 (0.4)	0	1 (0.2)
Timolol Maleate	0	1 (0.4)	1 (0.2)
Travopost/Timolol	1 (0.4)	0	1 (0.2)
ANTIGOUT PREPARATIONS	16 (6.7)	20 (8.6)	36 (7.6)
Allopurinol	11 (4.6)	15 (6.5)	26 (5.5)
Colchicine	2 (0.8)	1 (0.4)	3 (0.6)
Febuxostat	0	2 (0.9)	2 (0.4)
Adenuric	1 (0.4)	0	1 (0.2)
Allopurinolo	0	1 (0.4)	1 (0.2)
Alloril	0	1 (0.4)	1 (0.2)
Allpurinol	1 (0.4)	0	1 (0.2)
Milurit	0	1 (0.4)	1 (0.2)
Milurit / Allopurinol	1 (0.4)	0	1 (0.2)
Urosin	0	1 (0.4)	1 (0.2)
ANTIHISTAMINES FOR SYSTEMIC USE	16 (6.7)	13 (5.6)	29 (6.2)
Fenistil	2 (0.8)	2 (0.9)	4 (0.8)
Desloratadine	2 (0.8)	1 (0.4)	3 (0.6)
Atosil	0	2 (0.9)	2 (0.4)
Cetirizine	1 (0.4)	1 (0.4)	2 (0.4)
Loratadine	1 (0.4)	1 (0.4)	2 (0.4)
Promethazine	1 (0.4)	1 (0.4)	2 (0.4)
Aerius	1 (0.4)	0	1 (0.2)
Ceterizin	1 (0.4)	0	1 (0.2)
Cetirizin	1 (0.4)	0	1 (0.2)
Clatra	1 (0.4)	0	1 (0.2)
Clemastin	0	1 (0.4)	1 (0.2)
Clemastin Fumarat	1 (0.4)	0	1 (0.2)
Desloratatin	1 (0.4)	0	1 (0.2)
Desloratidin	1 (0.4)	0	1 (0.2)
Dexclorferniramina	0	1 (0.4)	1 (0.2)
Dibondrin	1 (0.4)	0	1 (0.2)
Dimetinden	0	1 (0.4)	1 (0.2)
Ebastine	0	1 (0.4)	1 (0.2)
Fexofenadin	1 (0.4)	0	1 (0.2)
Loratadin	1 (0.4)	0	1 (0.2)
Mepyramine	0	1 (0.4)	1 (0.2)
Trimethobenzamide	0	1 (0.4)	1 (0.2)
Zyrtex	1 (0.4)	0	1 (0.2)
ANTIINFECTIVES	3 (1.3)	4 (1.7)	7 (1.5)
Chloramfenicol	0	1 (0.4)	1 (0.2)
Chloramphenicol 5%	0	1 (0.4)	1 (0.2)
Ciprofloxacin Ophthalmic Bilaterally	1 (0.4)	0	1 (0.2)
Gentamicin	0	1 (0.4)	1 (0.2)
Oflocet	0	1 (0.4)	1 (0.2)
Ofloxacine	1 (0.4)	0	1 (0.2)
Quinofree	1 (0.4)	0	1 (0.2)
ANTIINFECTIVES AND ANTISEPTICS, EXCL. COMBINATIONS WITH CORTICOSTEROIDS	2 (0.8)	0	2 (0.4)
Ampho-Moronal	1 (0.4)	0	1 (0.2)
Canesten Gyn Labiau	1 (0.4)	0	1 (0.2)
Polygynax	1 (0.4)	0	1 (0.2)

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ANTIINFLAMMATORY AGENTS	1 (0.4)	1 (0.4)	2 (0.4)
Dexamethason	1 (0.4)	0	1 (0.2)
Ozurdex	0	1 (0.4)	1 (0.2)
ANTIINFLAMMATORY AGENTS AND ANTIINFECTIVES IN COMBINATION	2 (0.8)	0	2 (0.4)
Sterdex	1 (0.4)	0	1 (0.2)
Tobradex	1 (0.4)	0	1 (0.2)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	17 (7.1)	6 (2.6)	23 (4.9)
Ibuprofen	9 (3.8)	4 (1.7)	13 (2.8)
Diclobene	1 (0.4)	1 (0.4)	2 (0.4)
Diclofenac	2 (0.8)	0	2 (0.4)
Dexketoprofen	1 (0.4)	0	1 (0.2)
Glucosamine Chondroitin	0	1 (0.4)	1 (0.2)
Ibuprofene	1 (0.4)	0	1 (0.2)
Meloxicam	1 (0.4)	0	1 (0.2)
Naproxen	1 (0.4)	0	1 (0.2)
Parecoxib	1 (0.4)	0	1 (0.2)
Seractil	1 (0.4)	0	1 (0.2)
Voltaren (Diclofenac Natrium)	1 (0.4)	0	1 (0.2)
ANTIMETABOLITES	0	1 (0.4)	1 (0.2)
Methotrexate	0	1 (0.4)	1 (0.2)
ANTIMYCOTICS FOR SYSTEMIC USE	4 (1.7)	1 (0.4)	5 (1.1)
Fluconazol	1 (0.4)	1 (0.4)	2 (0.4)
Fluconazole	2 (0.8)	0	2 (0.4)
Micafungin	1 (0.4)	0	1 (0.2)
ANTIPROPULSIVES	3 (1.3)	2 (0.9)	5 (1.1)
Imodium	2 (0.8)	0	2 (0.4)
Loperamide	1 (0.4)	1 (0.4)	2 (0.4)
Loperamide Hcl	0	1 (0.4)	1 (0.2)
Fenistil	1 (0.4)	0	1 (0.2)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	1 (0.4)	0	1 (0.2)
Prochlorperazine	0	1 (0.4)	1 (0.2)
ANTIPSYCHOTICS	59 (24.7)	55 (23.7)	114 (24.2)
Melperon	16 (6.7)	16 (6.9)	32 (6.8)
Quetiapin	7 (2.9)	13 (5.6)	20 (4.2)
Haloperidol	8 (3.3)	10 (4.3)	18 (3.8)
Risperidon	9 (3.8)	9 (3.9)	18 (3.8)
Quetiapine	6 (2.5)	7 (3.0)	13 (2.8)
Seroquel	7 (2.9)	4 (1.7)	11 (2.3)
Haldol	3 (1.3)	2 (0.9)	5 (1.1)
Pipamperon	4 (1.7)	1 (0.4)	5 (1.1)
Quetialan	3 (1.3)	2 (0.9)	5 (1.1)
Risperidone	3 (1.3)	2 (0.9)	5 (1.1)
Olanzapine	3 (1.3)	1 (0.4)	4 (0.8)
Risperdal	1 (0.4)	2 (0.9)	3 (0.6)
Dipiperon	2 (0.8)	0	2 (0.4)
Loxapine	1 (0.4)	1 (0.4)	2 (0.4)
Methotrimeprazine	1 (0.4)	1 (0.4)	2 (0.4)

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Quetiapina	2 (0.8)	0	2 (0.4)
Buronil	1 (0.4)	0	1 (0.2)
Clothiapine	1 (0.4)	0	1 (0.2)
Clotiapine	0	1 (0.4)	1 (0.2)
Haldol 2mg/Ml Drops	0	1 (0.4)	1 (0.2)
Halidol	1 (0.4)	0	1 (0.2)
Haloperidol Lactate	0	1 (0.4)	1 (0.2)
Ketipinor	1 (0.4)	0	1 (0.2)
Lanolept	1 (0.4)	0	1 (0.2)
Melneurin	0	1 (0.4)	1 (0.2)
Melperon Drg	0	1 (0.4)	1 (0.2)
Melperon Lsg	0	1 (0.4)	1 (0.2)
Promazina	0	1 (0.4)	1 (0.2)
Promazine	1 (0.4)	0	1 (0.2)
Quatiapin	0	1 (0.4)	1 (0.2)
Quetiapin Xr	0	1 (0.4)	1 (0.2)
Quetiapine Fumarate	0	1 (0.4)	1 (0.2)
Quietapine	1 (0.4)	0	1 (0.2)
Sulpiride	0	1 (0.4)	1 (0.2)
Tiapridal	1 (0.4)	0	1 (0.2)
Tiapride	0	1 (0.4)	1 (0.2)
ANTISEPTICS AND DISINFECTANTS	2 (0.8)	0	2 (0.4)
Dermalex	1 (0.4)	0	1 (0.2)
Eosina	1 (0.4)	0	1 (0.2)
Isobetadine	1 (0.4)	0	1 (0.2)
ANTITHROMBOTIC AGENTS	190 (79.5)	172 (74.1)	362 (76.9)
Enoxaparin	51 (21.3)	46 (19.8)	97 (20.6)
Heparin	19 (7.9)	23 (9.9)	42 (8.9)
Clexane	18 (7.5)	12 (5.2)	30 (6.4)
Enoxaparine	12 (5.0)	17 (7.3)	29 (6.2)
Tinzaparin	13 (5.4)	11 (4.7)	24 (5.1)
Lovenox	13 (5.4)	10 (4.3)	23 (4.9)
Apixaban	9 (3.8)	12 (5.2)	21 (4.5)
Aspirin	11 (4.6)	3 (1.3)	14 (3.0)
Fraxiparine	9 (3.8)	4 (1.7)	13 (2.8)
Certoparin	5 (2.1)	5 (2.2)	10 (2.1)
Clopidogrel	7 (2.9)	3 (1.3)	10 (2.1)
Dalteparin	5 (2.1)	5 (2.2)	10 (2.1)
Fragmin	7 (2.9)	2 (0.9)	9 (1.9)
Nadroparine	3 (1.3)	5 (2.2)	8 (1.7)
Eliquis	5 (2.1)	2 (0.9)	7 (1.5)
Innohep	4 (1.7)	3 (1.3)	7 (1.5)
Acetylsalicylic Acid	3 (1.3)	3 (1.3)	6 (1.3)
Rivaroxaban	2 (0.8)	4 (1.7)	6 (1.3)
Kardegic	4 (1.7)	1 (0.4)	5 (1.1)
Dabigatran	4 (1.7)	0	4 (0.8)
Fragmin P Forte	2 (0.8)	2 (0.9)	4 (0.8)
Pradaxa	3 (1.3)	1 (0.4)	4 (0.8)
Ass	3 (1.3)	0	3 (0.6)
Enoxaparin Natrium	2 (0.8)	1 (0.4)	3 (0.6)
Enoxaparina	1 (0.4)	2 (0.9)	3 (0.6)
Tinzaparin Natrium	1 (0.4)	2 (0.9)	3 (0.6)
Alteplase	1 (0.4)	1 (0.4)	2 (0.4)

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Apixiban	1 (0.4)	1 (0.4)	2 (0.4)
Arixtra	1 (0.4)	1 (0.4)	2 (0.4)
Dalteparine	2 (0.8)	0	2 (0.4)
Enoxaeparina	0	2 (0.9)	2 (0.4)
Enoxaparin Sodium	1 (0.4)	1 (0.4)	2 (0.4)
Heparin Sodium	0	2 (0.9)	2 (0.4)
Heparine	2 (0.8)	0	2 (0.4)
Micropirin	1 (0.4)	1 (0.4)	2 (0.4)
Mono-Embolex	2 (0.8)	0	2 (0.4)
Nadroparin	1 (0.4)	1 (0.4)	2 (0.4)
Nadroparine (Fraxiparine)	1 (0.4)	1 (0.4)	2 (0.4)
Xarelto	0	2 (0.9)	2 (0.4)
Acetyl Salicylic Acid (Aspirin)	1 (0.4)	0	1 (0.2)
Apixabane	0	1 (0.4)	1 (0.2)
Asa	1 (0.4)	0	1 (0.2)
Aspegic	1 (0.4)	0	1 (0.2)
Aspirin Cardio	1 (0.4)	0	1 (0.2)
Bemiparina	0	1 (0.4)	1 (0.2)
Calciparine	1 (0.4)	0	1 (0.2)
Clexan	1 (0.4)	0	1 (0.2)
Clexane Prefilled	0	1 (0.4)	1 (0.2)
Clexane- Enoxaparin	1 (0.4)	0	1 (0.2)
Clexane/Enoxaparin	1 (0.4)	0	1 (0.2)
Dalteparine 5.000	1 (0.4)	0	1 (0.2)
Deltaparin	1 (0.4)	0	1 (0.2)
Dipyridamole	1 (0.4)	0	1 (0.2)
Endoxaban	1 (0.4)	0	1 (0.2)
Endoxaparin	0	1 (0.4)	1 (0.2)
Enoksaparin	1 (0.4)	0	1 (0.2)
Enoxaparin Na	0	1 (0.4)	1 (0.2)
Enoxaparin Natrium 4000 Iu	0	1 (0.4)	1 (0.2)
Enoxaparin Natrium/ Clexane	1 (0.4)	0	1 (0.2)
Enoxaparin-Na	1 (0.4)	0	1 (0.2)
Enoxaparine Natrium	0	1 (0.4)	1 (0.2)
Enoxaparine Sodique	0	1 (0.4)	1 (0.2)
Enoxaparine, Lovenox 4000ui/0.4ml, Subcutaneous	0	1 (0.4)	1 (0.2)
Enoxaparine-Hexal	0	1 (0.4)	1 (0.2)
Enoxaperin	1 (0.4)	0	1 (0.2)
Enoxeparine (Lovenox) 4000ui	1 (0.4)	0	1 (0.2)
Fondaprinux	1 (0.4)	0	1 (0.2)
Fraxiparin	0	1 (0.4)	1 (0.2)
Ghemaxan	1 (0.4)	0	1 (0.2)
Heparin Bolus	0	1 (0.4)	1 (0.2)
Heparin Infusion	0	1 (0.4)	1 (0.2)
Heparin Lock	0	1 (0.4)	1 (0.2)
Heparin Perfusor	0	1 (0.4)	1 (0.2)
Heparin Preservative Free	0	1 (0.4)	1 (0.2)
Heparin Sodium Dextrose	0	1 (0.4)	1 (0.2)
Innohepp	0	1 (0.4)	1 (0.2)
Lovenox (Enoxaparin Natrium)	1 (0.4)	0	1 (0.2)
Lovenox 4000ui/0.4ml, Subcutaneous	1 (0.4)	0	1 (0.2)
Low Molecular Wave Heparin	1 (0.4)	0	1 (0.2)
Low Molecular Weight Heparin	1 (0.4)	0	1 (0.2)
Low Molecular Weight Heparine	0	1 (0.4)	1 (0.2)
Micropirin Tab 75 Mg	0	1 (0.4)	1 (0.2)

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Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Mono Embolex	1 (0.4)	0	1 (0.2)
Mono-Embolex 3000 E	0	1 (0.4)	1 (0.2)
Neoparin	1 (0.4)	0	1 (0.2)
Platelet	1 (0.4)	0	1 (0.2)
Plavix	0	1 (0.4)	1 (0.2)
Sodium Bemiparin	0	1 (0.4)	1 (0.2)
Thrombo Ass	0	1 (0.4)	1 (0.2)
Tpa-Tissue Plasminogen Activator	0	1 (0.4)	1 (0.2)
Ã‰noxaparine	0	1 (0.4)	1 (0.2)
ANTITHYROID PREPARATIONS	4 (1.7)	7 (3.0)	11 (2.3)
Natriumperchlorat	1 (0.4)	2 (0.9)	3 (0.6)
Carbimazol	0	2 (0.9)	2 (0.4)
Thiamazol	0	2 (0.9)	2 (0.4)
Thiamazole	1 (0.4)	1 (0.4)	2 (0.4)
Methimazole	1 (0.4)	0	1 (0.2)
Thyrozol / Thiamazole	1 (0.4)	0	1 (0.2)
Tiamizol	0	1 (0.4)	1 (0.2)
ANTIVARICOSE THERAPY	2 (0.8)	2 (0.9)	4 (0.8)
Glycosaminoglycanopolysolfate	1 (0.4)	0	1 (0.2)
Heparinoid, 3 Mg/G	0	1 (0.4)	1 (0.2)
Hirudoid (Heparinoid)	0	1 (0.4)	1 (0.2)
Hirudoid Gel	1 (0.4)	0	1 (0.2)
Dimenhydrinat	0	1 (0.4)	1 (0.2)
ANTIVERTIGO PREPARATIONS	4 (1.7)	2 (0.9)	6 (1.3)
Betahistine	2 (0.8)	1 (0.4)	3 (0.6)
Betahistin	1 (0.4)	0	1 (0.2)
Vestibo / Betahistine	1 (0.4)	0	1 (0.2)
Cipralex	0	1 (0.4)	1 (0.2)
Pregabalin	0	1 (0.4)	1 (0.2)
Diazepam	8 (3.3)	7 (3.0)	15 (3.2)
ANXIOLYTICS	51 (21.3)	60 (25.9)	111 (23.6)
Lorazepam	17 (7.1)	24 (10.3)	41 (8.7)
Oxazepam	6 (2.5)	5 (2.2)	11 (2.3)
Alprazolam	3 (1.3)	5 (2.2)	8 (1.7)
Tavor	4 (1.7)	2 (0.9)	6 (1.3)
Temesta	3 (1.3)	2 (0.9)	5 (1.1)
Bromazepam	1 (0.4)	3 (1.3)	4 (0.8)
Loracepam	2 (0.8)	2 (0.9)	4 (0.8)
Vaben	2 (0.8)	2 (0.9)	4 (0.8)
Clonazepam	0	3 (1.3)	3 (0.6)
Paroxetine	1 (0.4)	2 (0.9)	3 (0.6)
Atarax	0	2 (0.9)	2 (0.4)
Seresta	2 (0.8)	0	2 (0.4)
Aprazolam	0	1 (0.4)	1 (0.2)
Ativan	0	1 (0.4)	1 (0.2)
Clomipramine	0	1 (0.4)	1 (0.2)
Diasepam	1 (0.4)	0	1 (0.2)
Etifoxine	0	1 (0.4)	1 (0.2)
Hydroxizine	1 (0.4)	0	1 (0.2)
Hydroxyzine Hcl	0	1 (0.4)	1 (0.2)
Lexaurin	1 (0.4)	0	1 (0.2)

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Lorazempam	0	1 (0.4)	1 (0.2)
Lorezepam	0	1 (0.4)	1 (0.2)
Lorivan Tab 1 Mg	1 (0.4)	0	1 (0.2)
Neurol (Alprazolam)	0	1 (0.4)	1 (0.2)
Pregabaline	0	1 (0.4)	1 (0.2)
Tavor / Lorazepam	1 (0.4)	0	1 (0.2)
Tavor Expidet	1 (0.4)	0	1 (0.2)
Tavor/ Lorazepam	1 (0.4)	0	1 (0.2)
Valium	1 (0.4)	0	1 (0.2)
Xanax	0	1 (0.4)	1 (0.2)
ARTERIOLAR SMOOTH MUSCLE, AGENTS ACTING ON	46 (19.2)	45 (19.4)	91 (19.3)
Hydralazine	18 (7.5)	21 (9.1)	39 (8.3)
Dihydralazin	14 (5.9)	11 (4.7)	25 (5.3)
Nepresol	3 (1.3)	10 (4.3)	13 (2.8)
Minoxidil	4 (1.7)	2 (0.9)	6 (1.3)
Lonolox	2 (0.8)	0	2 (0.4)
Dihydralatsiini	1 (0.4)	0	1 (0.2)
Dihydralazib	1 (0.4)	0	1 (0.2)
Dihydralazin / Nepresol	1 (0.4)	0	1 (0.2)
Dihydralazine	1 (0.4)	0	1 (0.2)
Dihydralazinsulfat	1 (0.4)	0	1 (0.2)
Hydralizine	1 (0.4)	0	1 (0.2)
Hydralzaine	0	1 (0.4)	1 (0.2)
Loniten	0	1 (0.4)	1 (0.2)
Nepresol (25mg/2ml)	1 (0.4)	0	1 (0.2)
Nepresol (Dihydralazine)	0	1 (0.4)	1 (0.2)
P-Dihydralazin	1 (0.4)	0	1 (0.2)
ASCORBIC ACID (VITAMIN C), INCL. COMBINATIONS	3 (1.3)	3 (1.3)	6 (1.3)
Vitamin C	2 (0.8)	2 (0.9)	4 (0.8)
Ascorbin Acid	0	1 (0.4)	1 (0.2)
Vtamin C	1 (0.4)	0	1 (0.2)
Aldosterone antagonists and other potassium-sparing agents	32 (13.4)	30 (12.9)	62 (13.2)
Spironolacton	10 (4.2)	11 (4.7)	21 (4.5)
Spironolactone	9 (3.8)	6 (2.6)	15 (3.2)
Aldactone	3 (1.3)	4 (1.7)	7 (1.5)
Eplerenon	1 (0.4)	2 (0.9)	3 (0.6)
Eplerenone	2 (0.8)	1 (0.4)	3 (0.6)
Luvion	0	2 (0.9)	2 (0.4)
Spirobene	2 (0.8)	0	2 (0.4)
Verospiron	2 (0.8)	0	2 (0.4)
Amiloride	1 (0.4)	0	1 (0.2)
Canrenone	0	1 (0.4)	1 (0.2)
Inspra Tab 25 Mg	0	1 (0.4)	1 (0.2)
Spironaolacton	1 (0.4)	0	1 (0.2)
Spironocaltone	0	1 (0.4)	1 (0.2)
Spironolactone (Aldactone)	0	1 (0.4)	1 (0.2)
Spironolactone Eg	1 (0.4)	0	1 (0.2)
Spironolattone	0	1 (0.4)	1 (0.2)
Angiotensin II receptor blockers (ARBs), combinations	11 (4.6)	9 (3.9)	20 (4.2)
Entresto	4 (1.7)	1 (0.4)	5 (1.1)
Candeblo Plus 32/12.5 Mg	1 (0.4)	0	1 (0.2)

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Candesartan Hct 32/25 Mg	1 (0.4)	0	1 (0.2)
Co-Valsacor / Valsartan 160 Mg + Hydrochlorotiazide 25 Mg	1 (0.4)	0	1 (0.2)
Exforge	0	1 (0.4)	1 (0.2)
Exforge (Amlodipine+valsartan)	0	1 (0.4)	1 (0.2)
Exforge 5/160 Mg	1 (0.4)	0	1 (0.2)
Exforge Hct (5 Mg Amlodipine, 12,5 Mg Hydrochlorothiazide, And 160 Mg Valsartan)	0	1 (0.4)	1 (0.2)
Exforge Tab 10mg/160 Mg	0	1 (0.4)	1 (0.2)
Hydrochlorothiazide And Candesartan Comb (12,5 Mg /16 Mg)	1 (0.4)	0	1 (0.2)
Olmetec Plus	0	1 (0.4)	1 (0.2)
Pemzek Plus	0	1 (0.4)	1 (0.2)
Sacubitril-Valsartan 24-26mg	0	1 (0.4)	1 (0.2)
Sacubitril-Valsartan 49-51mg	0	1 (0.4)	1 (0.2)
Sacubitril/Valsartan (97/103 Mg)	0	1 (0.4)	1 (0.2)
Sacubitril/Valsartan 97mg/103mg	0	1 (0.4)	1 (0.2)
Telam 40+5 / Telmisartan 40mg + Amlodipine 5mg	1 (0.4)	0	1 (0.2)
Telmisartan-Hydrochlorthiazid	1 (0.4)	0	1 (0.2)
Teveten Plus	1 (0.4)	0	1 (0.2)
Valsartan (In Combination With Amlodipin)	1 (0.4)	0	1 (0.2)
Angiotensin II receptor blockers (ARBs), plain	92 (38.5)	63 (27.2)	155 (32.9)
Candesartan	46 (19.2)	29 (12.5)	75 (15.9)
Losartan	18 (7.5)	10 (4.3)	28 (5.9)
Valsartan	14 (5.9)	10 (4.3)	24 (5.1)
Irbesartan	4 (1.7)	7 (3.0)	11 (2.3)
Olmesartan	4 (1.7)	5 (2.2)	9 (1.9)
Telmisartan	4 (1.7)	3 (1.3)	7 (1.5)
Candersartan	2 (0.8)	0	2 (0.4)
Losartankalium	2 (0.8)	0	2 (0.4)
Aprovel	1 (0.4)	0	1 (0.2)
Candecor	1 (0.4)	0	1 (0.2)
Candsartan	0	1 (0.4)	1 (0.2)
Cozaar	0	1 (0.4)	1 (0.2)
Diovan	1 (0.4)	0	1 (0.2)
Karbis (Candesartan)	0	1 (0.4)	1 (0.2)
Lorsartan	0	1 (0.4)	1 (0.2)
Losardex	0	1 (0.4)	1 (0.2)
Micardis	1 (0.4)	0	1 (0.2)
Ocsaar	1 (0.4)	0	1 (0.2)
Olmesartan Medoxomil	0	1 (0.4)	1 (0.2)
Olmesartan/ Medoxomil	0	1 (0.4)	1 (0.2)
Telmisartane	0	1 (0.4)	1 (0.2)
Telmisartã¡n	1 (0.4)	0	1 (0.2)
Teveten	1 (0.4)	0	1 (0.2)
Valsacor	1 (0.4)	0	1 (0.2)
BACTERIAL VACCINES	0	1 (0.4)	1 (0.2)
Diphthria-Tetanus Toxoid Cd 0.5 Ml	0	1 (0.4)	1 (0.2)
BELLADONNA AND DERIVATIVES, PLAIN	3 (1.3)	4 (1.7)	7 (1.5)
Scopolamine Hydrobromide	1 (0.4)	1 (0.4)	2 (0.4)
Buscapine	0	1 (0.4)	1 (0.2)
Buscopan	1 (0.4)	0	1 (0.2)
Butylscopolamin	0	1 (0.4)	1 (0.2)
Butylscopolaminiumbromid	1 (0.4)	0	1 (0.2)
Scopolaminebutyl	0	1 (0.4)	1 (0.2)

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BETA BLOCKING AGENTS	175 (73.2)	172 (74.1)	347 (73.7)
Bisoprolol	55 (23.0)	66 (28.4)	121 (25.7)
Metoprolol	55 (23.0)	51 (22.0)	106 (22.5)
Labetalol	31 (13.0)	33 (14.2)	64 (13.6)
Atenolol	7 (2.9)	5 (2.2)	12 (2.5)
Carvedilol	5 (2.1)	7 (3.0)	12 (2.5)
Nebivolol	5 (2.1)	6 (2.6)	11 (2.3)
Trandate	7 (2.9)	3 (1.3)	10 (2.1)
Cardiloc	5 (2.1)	3 (1.3)	8 (1.7)
Labetolol	5 (2.1)	2 (0.9)	7 (1.5)
Sotalol	5 (2.1)	2 (0.9)	7 (1.5)
Concor	1 (0.4)	4 (1.7)	5 (1.1)
Metoprololo	1 (0.4)	4 (1.7)	5 (1.1)
Normalol	3 (1.3)	2 (0.9)	5 (1.1)
Bisoprololo	2 (0.8)	2 (0.9)	4 (0.8)
Metoprolol Tartrate	2 (0.8)	2 (0.9)	4 (0.8)
Metoprololsuccinat	3 (1.3)	1 (0.4)	4 (0.8)
Bisoce	3 (1.3)	0	3 (0.6)
Bisoprolol Fumarate	3 (1.3)	0	3 (0.6)
Beloc Zok Mite	1 (0.4)	1 (0.4)	2 (0.4)
Bisohexal	1 (0.4)	1 (0.4)	2 (0.4)
Bisoprolol Fumarat	1 (0.4)	1 (0.4)	2 (0.4)
Concor Cor	1 (0.4)	1 (0.4)	2 (0.4)
Metoprolol Succinaat	2 (0.8)	0	2 (0.4)
Metorpolol	1 (0.4)	1 (0.4)	2 (0.4)
Propanolol	1 (0.4)	1 (0.4)	2 (0.4)
Acebutolol	0	1 (0.4)	1 (0.2)
Albetol	1 (0.4)	0	1 (0.2)
Beloc-Zok Mite	0	1 (0.4)	1 (0.2)
Betaloc	0	1 (0.4)	1 (0.2)
Betaxolol	0	1 (0.4)	1 (0.2)
Bisocard	1 (0.4)	0	1 (0.2)
Bisocard/Bisoprolol	1 (0.4)	0	1 (0.2)
Bisoprolol 1,25 Mg	0	1 (0.4)	1 (0.2)
Bisoprolol 2.5	1 (0.4)	0	1 (0.2)
Bisoprolol Fumarate Tab 5 Mg	0	1 (0.4)	1 (0.2)
Bisoprolol Furmate (Cardiloc)	0	1 (0.4)	1 (0.2)
Bisoprolol Mylan	1 (0.4)	0	1 (0.2)
Bisprolol	1 (0.4)	0	1 (0.2)
Bloxazoc	1 (0.4)	0	1 (0.2)
Cardensiel	1 (0.4)	0	1 (0.2)
Cardiloc Tab 2.5	0	1 (0.4)	1 (0.2)
Cardiloc- Bisoprolol	1 (0.4)	0	1 (0.2)
Carvidilol	0	1 (0.4)	1 (0.2)
Celiprolol	0	1 (0.4)	1 (0.2)
Emconcor	1 (0.4)	0	1 (0.2)
Esmolol	1 (0.4)	0	1 (0.2)
Labetalol Hydrochloride	1 (0.4)	0	1 (0.2)
Labetalol Infusion	1 (0.4)	0	1 (0.2)
Labetolol Infusion (Pump)	1 (0.4)	0	1 (0.2)
Lokren	1 (0.4)	0	1 (0.2)
Meto Hexal Succ	1 (0.4)	0	1 (0.2)
Meto Zerok (Metoprolol)	1 (0.4)	0	1 (0.2)
Metoprlolsuccinat	0	1 (0.4)	1 (0.2)

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Metoprol	1 (0.4)	0	1 (0.2)
Metoprolol (Retard)	1 (0.4)	0	1 (0.2)
Metoprolol Succ	0	1 (0.4)	1 (0.2)
Metoprolol Succinat	1 (0.4)	0	1 (0.2)
Metoprolol Succinat 47.5 Mg Ret	0	1 (0.4)	1 (0.2)
Metoprolol Tartraat	1 (0.4)	0	1 (0.2)
Metoprolol Tartrat	0	1 (0.4)	1 (0.2)
Metoprolole Tartrtate	0	1 (0.4)	1 (0.2)
Metorprolol	1 (0.4)	0	1 (0.2)
Metropolol	0	1 (0.4)	1 (0.2)
Metroprolol	0	1 (0.4)	1 (0.2)
Metroprololsuccinat	1 (0.4)	0	1 (0.2)
Monocor	1 (0.4)	0	1 (0.2)
Neobloc	1 (0.4)	0	1 (0.2)
Sobycor (Bisoprolol)	0	1 (0.4)	1 (0.2)
Sotalolo	0	1 (0.4)	1 (0.2)
BETA BLOCKING AGENTS AND THIAZIDES	3 (1.3)	1 (0.4)	4 (0.8)
Emcoretic	1 (0.4)	0	1 (0.2)
Lodoz	1 (0.4)	0	1 (0.2)
Seloken Ret.	1 (0.4)	0	1 (0.2)
Seloken Retard	0	1 (0.4)	1 (0.2)
BETA-LACTAM ANTIBACTERIALS, PENICILLINS	100 (41.8)	85 (36.6)	185 (39.3)
Piperacillin	10 (4.2)	11 (4.7)	21 (4.5)
Tazobactam	9 (3.8)	11 (4.7)	20 (4.2)
Ampicillin	10 (4.2)	7 (3.0)	17 (3.6)
Piperacillin/Tazobactam	11 (4.6)	3 (1.3)	14 (3.0)
Amoxicillin	4 (1.7)	9 (3.9)	13 (2.8)
Sulbactam	6 (2.5)	6 (2.6)	12 (2.5)
Tazobac	4 (1.7)	6 (2.6)	10 (2.1)
Augmentin	6 (2.5)	3 (1.3)	9 (1.9)
Unacid	3 (1.3)	6 (2.6)	9 (1.9)
Clavulanic Acid	3 (1.3)	5 (2.2)	8 (1.7)
Unasyn	4 (1.7)	4 (1.7)	8 (1.7)
Pivmecillinam	4 (1.7)	1 (0.4)	5 (1.1)
Tazocin	2 (0.8)	3 (1.3)	5 (1.1)
Ampicillin/Sulbactam	4 (1.7)	0	4 (0.8)
Amoxiciline-Clavulanic	1 (0.4)	2 (0.9)	3 (0.6)
Amoxicillin Clavulanate	3 (1.3)	0	3 (0.6)
Amoxicilline	1 (0.4)	2 (0.9)	3 (0.6)
Piperacillin-Tazobactam	1 (0.4)	2 (0.9)	3 (0.6)
Piperacillin/ Tazobactam	2 (0.8)	1 (0.4)	3 (0.6)
Piperacillina/Tazobactam	1 (0.4)	2 (0.9)	3 (0.6)
Unasyn (Sulbactam+ampicillin)	3 (1.3)	0	3 (0.6)
Amoxicillin And Clavulanic Acid	1 (0.4)	1 (0.4)	2 (0.4)
Amoxicillin/Clavulanic Acid	2 (0.8)	0	2 (0.4)
Amoxicillina/Acido Clavulanico	0	2 (0.9)	2 (0.4)
Amoxiclav	1 (0.4)	1 (0.4)	2 (0.4)
Clavulan Acid	0	2 (0.9)	2 (0.4)
Piperacilin/Tazobactam	2 (0.8)	0	2 (0.4)
Piperacillin Tazobactam	1 (0.4)	1 (0.4)	2 (0.4)
Sultamicillin	2 (0.8)	0	2 (0.4)
Ac. Clavulanique	1 (0.4)	0	1 (0.2)
Acide Clavulanique	1 (0.4)	0	1 (0.2)

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Amixicillin	0	1 (0.4)	1 (0.2)
Amoksiklav	0	1 (0.4)	1 (0.2)
Amoxacillin	1 (0.4)	0	1 (0.2)
Amoxicilin	1 (0.4)	0	1 (0.2)
Amoxicilin-Clavulanic	0	1 (0.4)	1 (0.2)
Amoxicilina	0	1 (0.4)	1 (0.2)
Amoxiciline	1 (0.4)	0	1 (0.2)
Amoxiciline Clavulanic	0	1 (0.4)	1 (0.2)
Amoxiciline-Clavulanic Acid	0	1 (0.4)	1 (0.2)
Amoxicillilna/Ac Clavulanico	1 (0.4)	0	1 (0.2)
Amoxicillin + Clavulanic Acid 1g/200mg	0	1 (0.4)	1 (0.2)
Amoxicillin Clavulanic	0	1 (0.4)	1 (0.2)
Amoxicillin Clavulanic Acid (1 Gr/200mg)	0	1 (0.4)	1 (0.2)
Amoxicillin-Clavulanic Acid	1 (0.4)	0	1 (0.2)
Amoxicillin/Clavulanate	0	1 (0.4)	1 (0.2)
Amoxicillin/Clavulanate (875mg/125mg)	0	1 (0.4)	1 (0.2)
Amoxicillin/Clavulanate 1g/250mg	0	1 (0.4)	1 (0.2)
Amoxicillin/Clavulanate 2g/200mg	0	1 (0.4)	1 (0.2)
Amoxicillin/Clavulanic	0	1 (0.4)	1 (0.2)
Amoxicillina/Ac Clavulanico	0	1 (0.4)	1 (0.2)
Amoxicilline + Acide Clavulanique	0	1 (0.4)	1 (0.2)
Amoxicilline + Clavulanique Acide 1g/125mg, Sachet	1 (0.4)	0	1 (0.2)
Amoxicilline + Clavulanique Acide 1g/200ml	1 (0.4)	0	1 (0.2)
Amoxicilline Clavulanic Acid	0	1 (0.4)	1 (0.2)
Amoxicilline/Clavulaanzuur	0	1 (0.4)	1 (0.2)
Amoxicilline/Clavulaanzuur 500/125 Mg	0	1 (0.4)	1 (0.2)
Amoxiclav 1g/125mg	1 (0.4)	0	1 (0.2)
Amoxiclav Sandoz	1 (0.4)	0	1 (0.2)
Amoxin	1 (0.4)	0	1 (0.2)
Ampicillin-Sublactam	1 (0.4)	0	1 (0.2)
Ampicillin/Sulbactam Kabi 1000mg/500mg	1 (0.4)	0	1 (0.2)
Amxiciline-Clavulanic	0	1 (0.4)	1 (0.2)
Antibiose With Piperacillin/Tazobactam	1 (0.4)	0	1 (0.2)
Augmentin (Amoxicillin, Clavulan-Acid)	1 (0.4)	0	1 (0.2)
Augmentin 1g	0	1 (0.4)	1 (0.2)
Augmentine	0	1 (0.4)	1 (0.2)
Benzylpenicillin	0	1 (0.4)	1 (0.2)
Clavulonacid	0	1 (0.4)	1 (0.2)
Cloxaciline	0	1 (0.4)	1 (0.2)
Co-Amoxicilin	1 (0.4)	0	1 (0.2)
Co-Amoxicillin	1 (0.4)	0	1 (0.2)
Co-Amoxiclav	1 (0.4)	0	1 (0.2)
Co-Amoxiclav Injection	0	1 (0.4)	1 (0.2)
Flucloxacillin	0	1 (0.4)	1 (0.2)
Flucloxacilline	1 (0.4)	0	1 (0.2)
Methicillin	1 (0.4)	0	1 (0.2)
Peperacillin/ Tazobactam	0	1 (0.4)	1 (0.2)
Pip-Tazo	1 (0.4)	0	1 (0.2)
Piperac/Tazobac	0	1 (0.4)	1 (0.2)
Piperacil./Tazobac. "stragen"	1 (0.4)	0	1 (0.2)
Piperacilin	0	1 (0.4)	1 (0.2)
Piperacilin-Tazobactam	1 (0.4)	0	1 (0.2)
Piperacilina-Tazobactam (4gr/250mg)	1 (0.4)	0	1 (0.2)
Piperacilina/Tazobactam	1 (0.4)	0	1 (0.2)
Piperaciline Tazobactam	0	1 (0.4)	1 (0.2)

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Piperaciline-Tazobactam	0	1 (0.4)	1 (0.2)
Piperacillin & Tazobactam	1 (0.4)	0	1 (0.2)
Piperacillin + Tazobac	1 (0.4)	0	1 (0.2)
Piperacillin / Tazobactam	0	1 (0.4)	1 (0.2)
Piperacillin / Tazobactam 4 /0,5	1 (0.4)	0	1 (0.2)
Piperacillin Tazobactum	1 (0.4)	0	1 (0.2)
Piperacillin+taxzobac	1 (0.4)	0	1 (0.2)
Piperacillin+tazobactam	1 (0.4)	0	1 (0.2)
Piperacillin/ Tazobact	1 (0.4)	0	1 (0.2)
Piperacillin/Tazobac	1 (0.4)	0	1 (0.2)
Piperacillin/Tazobactam (4g/0.5 G)	0	1 (0.4)	1 (0.2)
Piperacillin/Tazobactam 4/0,5 G	0	1 (0.4)	1 (0.2)
Piperacillin4g /Tazobactam 0.5g	0	1 (0.4)	1 (0.2)
Piperacillina-Tazobactam	1 (0.4)	0	1 (0.2)
Piperacilline	1 (0.4)	0	1 (0.2)
Piperacilline/Tazobactam	0	1 (0.4)	1 (0.2)
Pipercillin	1 (0.4)	0	1 (0.2)
Selexid	1 (0.4)	0	1 (0.2)
Sulbactam/Ampicilin	1 (0.4)	0	1 (0.2)
Sulbactan	1 (0.4)	0	1 (0.2)
Tacobac	1 (0.4)	0	1 (0.2)
Tacobactam	1 (0.4)	0	1 (0.2)
Tazo-Dip Avenir	1 (0.4)	0	1 (0.2)
Tazocel	0	1 (0.4)	1 (0.2)
Tazocillin	1 (0.4)	0	1 (0.2)
Tazocilline	0	1 (0.4)	1 (0.2)
Unacid In Sodium Chloride	1 (0.4)	0	1 (0.2)
Unasyn (Ampicillin & Sulbactam)	1 (0.4)	0	1 (0.2)
Zosyn	1 (0.4)	0	1 (0.2)
BILE THERAPY	2 (0.8)	3 (1.3)	5 (1.1)
Ursofalk	1 (0.4)	2 (0.9)	3 (0.6)
Acido Ursodeossicolico	0	1 (0.4)	1 (0.2)
Deursil	1 (0.4)	0	1 (0.2)
BLOOD AND RELATED PRODUCTS	9 (3.8)	10 (4.3)	19 (4.0)
Albumin	3 (1.3)	0	3 (0.6)
Erythrocyte Concentrate	1 (0.4)	1 (0.4)	2 (0.4)
Albiomin 20%	0	1 (0.4)	1 (0.2)
Albumina	0	1 (0.4)	1 (0.2)
Alburex	1 (0.4)	0	1 (0.2)
Blood Transfusions	0	1 (0.4)	1 (0.2)
Erythrozyteconcentrates	0	1 (0.4)	1 (0.2)
Ffp	1 (0.4)	0	1 (0.2)
Humanalbumin	1 (0.4)	0	1 (0.2)
Humanalbumin 20%	0	1 (0.4)	1 (0.2)
Packed Blood	0	1 (0.4)	1 (0.2)
Packed Erytrocytes	0	1 (0.4)	1 (0.2)
Platelet Concentrate	0	1 (0.4)	1 (0.2)
Platelets	0	1 (0.4)	1 (0.2)
Platelets Transfusion	0	1 (0.4)	1 (0.2)
Prbc Transfusion	1 (0.4)	0	1 (0.2)
Red Blood Cells	0	1 (0.4)	1 (0.2)
Red Cell Concentrate	1 (0.4)	0	1 (0.2)
Red Packed Cells	0	1 (0.4)	1 (0.2)

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BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	54 (22.6)	33 (14.2)	87 (18.5)
Metformin	25 (10.5)	16 (6.9)	41 (8.7)
Metformine	8 (3.3)	5 (2.2)	13 (2.8)
Sitagliptin	4 (1.7)	4 (1.7)	8 (1.7)
Empagliflozin	3 (1.3)	4 (1.7)	7 (1.5)
Januvia	4 (1.7)	1 (0.4)	5 (1.1)
Forxiga	2 (0.8)	1 (0.4)	3 (0.6)
Gliclazide	3 (1.3)	0	3 (0.6)
Glucophage	2 (0.8)	1 (0.4)	3 (0.6)
Linagliptin	2 (0.8)	1 (0.4)	3 (0.6)
Amaryl	1 (0.4)	1 (0.4)	2 (0.4)
Dapagliflozine	0	2 (0.9)	2 (0.4)
Glucomin	2 (0.8)	0	2 (0.4)
Janumet	2 (0.8)	0	2 (0.4)
Jardiance	2 (0.8)	0	2 (0.4)
Metformin Hydrochloride	1 (0.4)	1 (0.4)	2 (0.4)
Metformina	1 (0.4)	1 (0.4)	2 (0.4)
Daonil	1 (0.4)	0	1 (0.2)
Dapagliflozin	1 (0.4)	0	1 (0.2)
Dapaglifozin	1 (0.4)	0	1 (0.2)
Dulaglutide	0	1 (0.4)	1 (0.2)
Empagiflozin	1 (0.4)	0	1 (0.2)
Eucreas	0	1 (0.4)	1 (0.2)
Glibetic / Glimepiride	1 (0.4)	0	1 (0.2)
Glicazide	0	1 (0.4)	1 (0.2)
Gliclazid	1 (0.4)	0	1 (0.2)
Gliclizide	1 (0.4)	0	1 (0.2)
Glimeprid	1 (0.4)	0	1 (0.2)
Glimepririd	1 (0.4)	0	1 (0.2)
Glucomin- Metformin Hydrochloride	1 (0.4)	0	1 (0.2)
Inn-Empagliflozin	0	1 (0.4)	1 (0.2)
Jalra	0	1 (0.4)	1 (0.2)
Januet	1 (0.4)	0	1 (0.2)
Liraglutid	1 (0.4)	0	1 (0.2)
Metfogamma	0	1 (0.4)	1 (0.2)
Metforal	1 (0.4)	0	1 (0.2)
Metformax	1 (0.4)	0	1 (0.2)
Metformax (Metformin)	0	1 (0.4)	1 (0.2)
Metformine 1000mg	1 (0.4)	0	1 (0.2)
Metformine Mylan	1 (0.4)	0	1 (0.2)
Novonorm	1 (0.4)	0	1 (0.2)
Onglyza	1 (0.4)	0	1 (0.2)
Ozempic	1 (0.4)	0	1 (0.2)
Repaglinide	1 (0.4)	0	1 (0.2)
Saxagliptin	1 (0.4)	0	1 (0.2)
Siofor / Metformin	1 (0.4)	0	1 (0.2)
Sitaglipine	0	1 (0.4)	1 (0.2)
Sitagliplin	1 (0.4)	0	1 (0.2)
Sitagliptin + Metformin (50+850)	0	1 (0.4)	1 (0.2)
Sitagliptine	0	1 (0.4)	1 (0.2)
Stagid	1 (0.4)	0	1 (0.2)
Teva Gliclazide	1 (0.4)	0	1 (0.2)
Trajenta	0	1 (0.4)	1 (0.2)
Victoza	1 (0.4)	0	1 (0.2)

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Calcium Carbonate	2 (0.8)	5 (2.2)	7 (1.5)
CALCIUM	25 (10.5)	15 (6.5)	40 (8.5)
Calcium	8 (3.3)	2 (0.9)	10 (2.1)
Calciduran	3 (1.3)	1 (0.4)	4 (0.8)
Calciumcarbonat	2 (0.8)	0	2 (0.4)
Cal-D-Vita	0	1 (0.4)	1 (0.2)
Calcichew	1 (0.4)	0	1 (0.2)
Calcigran Forte	0	1 (0.4)	1 (0.2)
Calcium + Vitamin D 600/400	1 (0.4)	0	1 (0.2)
Calcium 600 + D	0	1 (0.4)	1 (0.2)
Calcium 600 Mg+vitamin D3 200 Tab 600 Mg /200iu	1 (0.4)	0	1 (0.2)
Calcium And Vitamin D	1 (0.4)	0	1 (0.2)
Calcium Carbonat	1 (0.4)	0	1 (0.2)
Calcium Carbonate_vitamin D3	1 (0.4)	0	1 (0.2)
Calcium Ion	1 (0.4)	0	1 (0.2)
Calcium/Vitd3	1 (0.4)	0	1 (0.2)
Calciumcarbonaat	1 (0.4)	0	1 (0.2)
Calciumcarbonaat/Colecalciferol	0	1 (0.4)	1 (0.2)
Calciumcarbonaat/Colecalciferol (Calci-Chew D3)	0	1 (0.4)	1 (0.2)
Caltrate	1 (0.4)	0	1 (0.2)
Carbonat Of Calcium	0	1 (0.4)	1 (0.2)
Citrocalcium	0	1 (0.4)	1 (0.2)
D-Vital Forte	0	1 (0.4)	1 (0.2)
Steovitd3 (Calcium1000/Colecalciferol800)	0	1 (0.4)	1 (0.2)
CAPILLARY STABILIZING AGENTS	0	1 (0.4)	1 (0.2)
Diosmine, Fraction Flavonoã¯que Purifiã©e Micronisã©e, Hespã©ridine	0	1 (0.4)	1 (0.2)
CARDIAC GLYCOSIDES	28 (11.7)	19 (8.2)	47 (10.0)
Digoxin	12 (5.0)	8 (3.4)	20 (4.2)
Digitoxin	7 (2.9)	4 (1.7)	11 (2.3)
Digoxine	4 (1.7)	6 (2.6)	10 (2.1)
Lanoxin	2 (0.8)	1 (0.4)	3 (0.6)
Acetyldigoxin	1 (0.4)	0	1 (0.2)
Digimerck	1 (0.4)	0	1 (0.2)
Digitalis	1 (0.4)	0	1 (0.2)
Digoxinum	1 (0.4)	0	1 (0.2)
Dixogin	0	1 (0.4)	1 (0.2)
Novodigal Mite	1 (0.4)	0	1 (0.2)
Suprarenin	1 (0.4)	0	1 (0.2)
CARDIAC STIMULANTS EXCL. CARDIAC GLYCOSIDES	25 (10.5)	26 (11.2)	51 (10.8)
Noradrenalin	8 (3.3)	4 (1.7)	12 (2.5)
Arterenol	2 (0.8)	5 (2.2)	7 (1.5)
Akrinor	1 (0.4)	5 (2.2)	6 (1.3)
Noradrenaline	3 (1.3)	3 (1.3)	6 (1.3)
Norepinephrine	4 (1.7)	2 (0.9)	6 (1.3)
Atropin	4 (1.7)	1 (0.4)	5 (1.1)
Norepinephrin	2 (0.8)	2 (0.9)	4 (0.8)
Phenylephrine	1 (0.4)	2 (0.9)	3 (0.6)
Atropine	0	2 (0.9)	2 (0.4)
Phenylepherin	1 (0.4)	1 (0.4)	2 (0.4)
Akrinor = Cafedrinhydrochlorid	1 (0.4)	0	1 (0.2)
Cafedrin	1 (0.4)	0	1 (0.2)

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Dobutamin	0	1 (0.4)	1 (0.2)
Efedrine	0	1 (0.4)	1 (0.2)
Effortil	0	1 (0.4)	1 (0.2)
Ephedrine	0	1 (0.4)	1 (0.2)
Epinephrine	0	1 (0.4)	1 (0.2)
Fenylefrine	0	1 (0.4)	1 (0.2)
Neo-Synephrine	1 (0.4)	0	1 (0.2)
Noradrenalin / Arterenol	1 (0.4)	0	1 (0.2)
Norepinephrin 0.02	1 (0.4)	0	1 (0.2)
Norepinephrine 4 Mg In Normal Saline 250 Ml Iv Infusion Premade	0	1 (0.4)	1 (0.2)
Noropinephrin	1 (0.4)	0	1 (0.2)
Phenylephrine Hcl	0	1 (0.4)	1 (0.2)
Phenylepinephrine	0	1 (0.4)	1 (0.2)
Phenylepineprine	0	1 (0.4)	1 (0.2)
CARDIOVASCULAR SYSTEM	1 (0.4)	0	1 (0.2)
Rb-82 Rubidium Chloride	1 (0.4)	0	1 (0.2)
CICATRIZANTS	1 (0.4)	0	1 (0.2)
Bepanthen / Privin	1 (0.4)	0	1 (0.2)
Dexamethason	0	5 (2.2)	5 (1.1)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	24 (10.0)	30 (12.9)	54 (11.5)
Prednisolon	9 (3.8)	6 (2.6)	15 (3.2)
Dexamethasone	3 (1.3)	2 (0.9)	5 (1.1)
Hydrocortisone	1 (0.4)	3 (1.3)	4 (0.8)
Metilprednisolone	1 (0.4)	3 (1.3)	4 (0.8)
Prednisone	1 (0.4)	3 (1.3)	4 (0.8)
Methylprednisolon	0	3 (1.3)	3 (0.6)
Prednison	2 (0.8)	0	2 (0.4)
Astonin H	0	1 (0.4)	1 (0.2)
Cortancyl	1 (0.4)	0	1 (0.2)
Decadron	1 (0.4)	0	1 (0.2)
Desamethasone	0	1 (0.4)	1 (0.2)
Dexacort (Dexamethasone)	1 (0.4)	0	1 (0.2)
Dexamentasone	0	1 (0.4)	1 (0.2)
Dexametasone	0	1 (0.4)	1 (0.2)
Dexamethasoni	1 (0.4)	0	1 (0.2)
Dexmethasone	0	1 (0.4)	1 (0.2)
Fortecortin	1 (0.4)	0	1 (0.2)
Fortecortin/ Dexamethason	1 (0.4)	0	1 (0.2)
Hydrocortison	1 (0.4)	0	1 (0.2)
Hydrokortison	1 (0.4)	0	1 (0.2)
Mephamesone	0	1 (0.4)	1 (0.2)
Methylprednisone	0	1 (0.4)	1 (0.2)
Metilprednisolona	0	1 (0.4)	1 (0.2)
Predinsolone	0	1 (0.4)	1 (0.2)
Prednisolone	0	1 (0.4)	1 (0.2)
Prednisolut (Prednisolon 21-Hydrogensuccinat)	1 (0.4)	0	1 (0.2)
Urbason	1 (0.4)	0	1 (0.2)
CORTICOSTEROIDS, COMBINATIONS WITH ANTIBIOTICS	0	1 (0.4)	1 (0.2)
Hydrocortison/Oxytetracycline/Polymyxine B Ear Droplets	0	1 (0.4)	1 (0.2)
Hydrocortisone	1 (0.4)	0	1 (0.2)

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Hydrocortison	1 (0.4)	0	1 (0.2)
CORTICOSTEROIDS, PLAIN	9 (3.8)	5 (2.2)	14 (3.0)
Betamethason	1 (0.4)	0	1 (0.2)
Clobetasol Propionate	1 (0.4)	0	1 (0.2)
Dermovate	1 (0.4)	0	1 (0.2)
Dermovate Cream 0.05% 25 Gm (Clobetasol Propionate)	1 (0.4)	0	1 (0.2)
Diflucortolone	1 (0.4)	0	1 (0.2)
Diprosone	0	1 (0.4)	1 (0.2)
Ecural	0	1 (0.4)	1 (0.2)
Fluticasone Propionate	0	1 (0.4)	1 (0.2)
Hydrocortisone Butyrate	1 (0.4)	0	1 (0.2)
Hydroval	1 (0.4)	0	1 (0.2)
Hydroval 0.2%	1 (0.4)	0	1 (0.2)
Lidex 0.05%	1 (0.4)	0	1 (0.2)
Mometasone Furoate 0.1%	1 (0.4)	0	1 (0.2)
Prednicarbat	0	1 (0.4)	1 (0.2)
Prednitop Creme	1 (0.4)	0	1 (0.2)
Soderm Creme	0	1 (0.4)	1 (0.2)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS	1 (0.4)	1 (0.4)	2 (0.4)
Benzonotate	0	1 (0.4)	1 (0.2)
Codein	1 (0.4)	0	1 (0.2)
Hydrocodone/Bit/Homatropine	0	1 (0.4)	1 (0.2)
Hydromet Syrup	0	1 (0.4)	1 (0.2)
Mupirocin	0	1 (0.4)	1 (0.2)
DECONGESTANTS AND OTHER NASAL PREPARATIONS FOR TOPICAL USE	8 (3.3)	6 (2.6)	14 (3.0)
Beclomethasone	0	1 (0.4)	1 (0.2)
Budesonide	1 (0.4)	0	1 (0.2)
Budesonide 1mg/2ml	1 (0.4)	0	1 (0.2)
Dexpanthenol	0	1 (0.4)	1 (0.2)
Fluticason-Proprionate	0	1 (0.4)	1 (0.2)
Ipratropium Bromide	1 (0.4)	0	1 (0.2)
Mometason	1 (0.4)	0	1 (0.2)
Mometasone Furoate	0	1 (0.4)	1 (0.2)
Nasonex	1 (0.4)	0	1 (0.2)
Nasonex Spray	0	1 (0.4)	1 (0.2)
Natriumchlorid	1 (0.4)	0	1 (0.2)
Otriven	1 (0.4)	0	1 (0.2)
Sodium Chloride Nasal Spray	1 (0.4)	0	1 (0.2)
Vitamin A Nose Drops	1 (0.4)	0	1 (0.2)
Xylomethazoline	0	1 (0.4)	1 (0.2)
Zymelin	1 (0.4)	0	1 (0.2)
DIGESTIVES, INCL. ENZYMES	0	1 (0.4)	1 (0.2)
Pankreas Pulver	0	1 (0.4)	1 (0.2)
DIRECT ACTING ANTIVIRALS	7 (2.9)	6 (2.6)	13 (2.8)
Remdesivir	3 (1.3)	1 (0.4)	4 (0.8)
Abacavir	0	1 (0.4)	1 (0.2)
Darunavir	0	1 (0.4)	1 (0.2)
Dolutegravir/Lamivudine (Dovato)	0	1 (0.4)	1 (0.2)
Lamivudine	0	1 (0.4)	1 (0.2)
Molnupiravir	1 (0.4)	0	1 (0.2)
Oseltamivir	0	1 (0.4)	1 (0.2)

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Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Paxlovid	0	1 (0.4)	1 (0.2)
Remedesivir	1 (0.4)	0	1 (0.2)
Valaciklovir	1 (0.4)	0	1 (0.2)
Valcyte	0	1 (0.4)	1 (0.2)
Zelitrex	1 (0.4)	0	1 (0.2)
Zovirax	1 (0.4)	0	1 (0.2)
DIURETICS AND POTASSIUM-SPARING AGENTS IN COMBINATION	1 (0.4)	3 (1.3)	4 (0.8)
Hydrochlorothiazide, Amiloride Hcl	1 (0.4)	0	1 (0.2)
Hydroclorothiazide/Amiloride	0	1 (0.4)	1 (0.2)
Lasitone	0	1 (0.4)	1 (0.2)
Triamterene-Hydrochlorothiazide	0	1 (0.4)	1 (0.2)
DOPAMINERGIC AGENTS	7 (2.9)	9 (3.9)	16 (3.4)
Dopicar	1 (0.4)	1 (0.4)	2 (0.4)
Madopar 100/25	1 (0.4)	1 (0.4)	2 (0.4)
Stalevo	1 (0.4)	1 (0.4)	2 (0.4)
Amantadine	0	1 (0.4)	1 (0.2)
Amantadinsulfat 0.04%	1 (0.4)	0	1 (0.2)
Benserazid	0	1 (0.4)	1 (0.2)
Benserazid Depot	0	1 (0.4)	1 (0.2)
Glepark	1 (0.4)	0	1 (0.2)
L-Dopa + Carbidopa 250/25mg, Tablet	1 (0.4)	0	1 (0.2)
Levodopa	0	1 (0.4)	1 (0.2)
Levodopa + Benserazide Hydrochloride (200+50)	0	1 (0.4)	1 (0.2)
Levodopa Depot Capsules	0	1 (0.4)	1 (0.2)
Levodopa/Carbidopa	1 (0.4)	0	1 (0.2)
Madopar 200/50	1 (0.4)	0	1 (0.2)
Modopar 250, Capsule	1 (0.4)	0	1 (0.2)
Neupro 4mg/24 H	1 (0.4)	0	1 (0.2)
Pk Merz	1 (0.4)	0	1 (0.2)
Pk-Merz	1 (0.4)	0	1 (0.2)
Prolopa	0	1 (0.4)	1 (0.2)
Rasagiline	0	1 (0.4)	1 (0.2)
Rasagiline Mesylate	1 (0.4)	0	1 (0.2)
Rotigotin	0	1 (0.4)	1 (0.2)
Rotigotine	0	1 (0.4)	1 (0.2)
Selegilin	0	1 (0.4)	1 (0.2)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	9 (3.8)	8 (3.4)	17 (3.6)
Prolia	3 (1.3)	0	3 (0.6)
Alendronate	1 (0.4)	1 (0.4)	2 (0.4)
Alendronic Acid	0	2 (0.9)	2 (0.4)
Denosumab	2 (0.8)	0	2 (0.4)
Alendronacid	0	1 (0.4)	1 (0.2)
Alendronat	1 (0.4)	0	1 (0.2)
Alendronate Sodium	0	1 (0.4)	1 (0.2)
Alendronic Acic	0	1 (0.4)	1 (0.2)
Alendronsäure	0	1 (0.4)	1 (0.2)
Fosalan	0	1 (0.4)	1 (0.2)
Ibandronic Acid	1 (0.4)	0	1 (0.2)
Risedronate	1 (0.4)	0	1 (0.2)
DRUGS FOR CONSTIPATION	109 (45.6)	97 (41.8)	206 (43.7)
Macrogol	28 (11.7)	18 (7.8)	46 (9.8)

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AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.3
Concomitant Medication
Safety Analysis Set

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Lactulose	18 (7.5)	19 (8.2)	37 (7.9)
Movicol	15 (6.3)	10 (4.3)	25 (5.3)
Bisacodyl	10 (4.2)	11 (4.7)	21 (4.5)
Senna	5 (2.1)	9 (3.9)	14 (3.0)
Polyethylene Glycol	5 (2.1)	8 (3.4)	13 (2.8)
Natriumpicosulfat	6 (2.5)	3 (1.3)	9 (1.9)
Sennosides	4 (1.7)	5 (2.2)	9 (1.9)
Dulcolax	5 (2.1)	2 (0.9)	7 (1.5)
Laxoberal	4 (1.7)	3 (1.3)	7 (1.5)
Avilac	4 (1.7)	2 (0.9)	6 (1.3)
Movicolon	3 (1.3)	3 (1.3)	6 (1.3)
Docusate	3 (1.3)	1 (0.4)	4 (0.8)
Forlax	3 (1.3)	1 (0.4)	4 (0.8)
Laxans	3 (1.3)	1 (0.4)	4 (0.8)
Molaxole	4 (1.7)	0	4 (0.8)
Polyethylene Glycol 3350	1 (0.4)	3 (1.3)	4 (0.8)
Bifiteral	1 (0.4)	2 (0.9)	3 (0.6)
Gangiden	3 (1.3)	0	3 (0.6)
Glycerin	1 (0.4)	2 (0.9)	3 (0.6)
Microlax	3 (1.3)	0	3 (0.6)
Naloxon	1 (0.4)	2 (0.9)	3 (0.6)
Peg 3350	3 (1.3)	0	3 (0.6)
Docusate Sodium	1 (0.4)	1 (0.4)	2 (0.4)
Duphalac	2 (0.8)	0	2 (0.4)
Eductyl	1 (0.4)	1 (0.4)	2 (0.4)
Emuliquen	0	2 (0.9)	2 (0.4)
Glycerine	2 (0.8)	0	2 (0.4)
Glycerol	1 (0.4)	1 (0.4)	2 (0.4)
Magrocol	0	2 (0.9)	2 (0.4)
Movivol	2 (0.8)	0	2 (0.4)
Natriumhydrogenphosphat	1 (0.4)	1 (0.4)	2 (0.4)
Normacol	2 (0.8)	0	2 (0.4)
Peglyte	1 (0.4)	1 (0.4)	2 (0.4)
Psyllium	1 (0.4)	1 (0.4)	2 (0.4)
Sodium Picosulfate	2 (0.8)	0	2 (0.4)
Avilac -Lactulose	1 (0.4)	0	1 (0.2)
Avilac Sol	1 (0.4)	0	1 (0.2)
Bifiteral Liquid	0	1 (0.4)	1 (0.2)
Bisacodyl / Bisacodyl	1 (0.4)	0	1 (0.2)
Bisacodyyl	0	1 (0.4)	1 (0.2)
Biscodyl	0	1 (0.4)	1 (0.2)
Bisocodyl	1 (0.4)	0	1 (0.2)
Casen Enema	0	1 (0.4)	1 (0.2)
Casen Rectal Enema	0	1 (0.4)	1 (0.2)
Castor Oil	0	1 (0.4)	1 (0.2)
Colace	0	1 (0.4)	1 (0.2)
Docusate Calcium	1 (0.4)	0	1 (0.2)
Docusate Senna	0	1 (0.4)	1 (0.2)
Docusate-Sinna	1 (0.4)	0	1 (0.2)
Enema	1 (0.4)	0	1 (0.2)
Enema Casen	0	1 (0.4)	1 (0.2)
Fibercon	1 (0.4)	0	1 (0.2)
Fleet Enema	1 (0.4)	0	1 (0.2)
Gangiden (Kcl, Macrogel 3350, Nacl, Natriumhydrogencarbonat)	0	1 (0.4)	1 (0.2)
Glycerin Suppository	0	1 (0.4)	1 (0.2)

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Glycerine Suppo	1 (0.4)	0	1 (0.2)
Glycerol / Bisacodyl	1 (0.4)	0	1 (0.2)
Glycerol/Bisacodyl	0	1 (0.4)	1 (0.2)
Glyoktyl	1 (0.4)	0	1 (0.2)
Hidroxid Of Magnesium	0	1 (0.4)	1 (0.2)
Klysma	0	1 (0.4)	1 (0.2)
Lactalose	1 (0.4)	0	1 (0.2)
Lactitol Monohydrate	0	1 (0.4)	1 (0.2)
Lactulosa	1 (0.4)	0	1 (0.2)
Lactulose "orifarm"	1 (0.4)	0	1 (0.2)
Lactulose (Avilac) 670mg/Ml	0	1 (0.4)	1 (0.2)
Lactulose 10 G, Sachet	0	1 (0.4)	1 (0.2)
Lactulose 66.7%	1 (0.4)	0	1 (0.2)
Lactulose, Mixture	1 (0.4)	0	1 (0.2)
Laevolac	1 (0.4)	0	1 (0.2)
Lax-A Day	1 (0.4)	0	1 (0.2)
Lax-A-Day	1 (0.4)	0	1 (0.2)
Laxadin	0	1 (0.4)	1 (0.2)
Laxadine	1 (0.4)	0	1 (0.2)
Laxbene	0	1 (0.4)	1 (0.2)
Laxoberon	0	1 (0.4)	1 (0.2)
Lebicarbon	0	1 (0.4)	1 (0.2)
Macrogol (Movicolon)	1 (0.4)	0	1 (0.2)
Macrogol 3350, Sachet	0	1 (0.4)	1 (0.2)
Macrogol/Salts (Movicolon)	0	1 (0.4)	1 (0.2)
Magnesium Hydroxide	0	1 (0.4)	1 (0.2)
Magnesium Oxide	1 (0.4)	0	1 (0.2)
Methylnaltrexonium	1 (0.4)	0	1 (0.2)
Mikroklist	0	1 (0.4)	1 (0.2)
Miralax	0	1 (0.4)	1 (0.2)
Mocrogol	1 (0.4)	0	1 (0.2)
Movical	1 (0.4)	0	1 (0.2)
Movicol (Magrogol)	0	1 (0.4)	1 (0.2)
Movicol Go	1 (0.4)	0	1 (0.2)
Movicol Pouch	1 (0.4)	0	1 (0.2)
Movicol/ Macrogol	0	1 (0.4)	1 (0.2)
Nartiumpicosulfate	1 (0.4)	0	1 (0.2)
Natrium Picosulfat	1 (0.4)	0	1 (0.2)
Natriumdihydrogenphosphat	1 (0.4)	0	1 (0.2)
Natriumfosfaten Klysma	1 (0.4)	0	1 (0.2)
Natriumpicos	0	1 (0.4)	1 (0.2)
Paraffin Oil	0	1 (0.4)	1 (0.2)
Phosphate	0	1 (0.4)	1 (0.2)
Phosphate Syrup	1 (0.4)	0	1 (0.2)
Polietilnglicol	1 (0.4)	0	1 (0.2)
Polyethyene Gycol 3350	0	1 (0.4)	1 (0.2)
Polyethylene Glycol 3350 Powder 17g	1 (0.4)	0	1 (0.2)
Rectal Easy Go	1 (0.4)	0	1 (0.2)
Senna Syrup	1 (0.4)	0	1 (0.2)
Sennoside	0	1 (0.4)	1 (0.2)
Senokot	0	1 (0.4)	1 (0.2)
Sodium Dibasic Phosphate	1 (0.4)	0	1 (0.2)
Sodium Dihydrogen Phosphate Monohydrate	0	1 (0.4)	1 (0.2)
Sodium Monobasic Phosphate (Fleet)	1 (0.4)	0	1 (0.2)
Sodium Phosphate Enema	0	1 (0.4)	1 (0.2)

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Sodium Phosphorus Klysma	0	1 (0.4)	1 (0.2)
Transipeg	0	1 (0.4)	1 (0.2)
Volcolon	1 (0.4)	0	1 (0.2)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	11 (4.6)	4 (1.7)	15 (3.2)
Glycopyrrolate	3 (1.3)	3 (1.3)	6 (1.3)
Espumisan	2 (0.8)	0	2 (0.4)
Glycopyrronium Bromide	1 (0.4)	0	1 (0.2)
Mebeverine	1 (0.4)	0	1 (0.2)
Papavarin	1 (0.4)	0	1 (0.2)
Phloroglucinol 80mg	1 (0.4)	0	1 (0.2)
Sab Simplex	0	1 (0.4)	1 (0.2)
Sab Simplexâ® 240 Mg Soft Capsules	1 (0.4)	0	1 (0.2)
Simeticone/Cuplaton	1 (0.4)	0	1 (0.2)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	152 (63.6)	135 (58.2)	287 (60.9)
Pantoprazol	56 (23.4)	68 (29.3)	124 (26.3)
Pantoprazole	25 (10.5)	24 (10.3)	49 (10.4)
Esomeprazol	19 (7.9)	11 (4.7)	30 (6.4)
Omeprazole	13 (5.4)	9 (3.9)	22 (4.7)
Omeprazol	7 (2.9)	12 (5.2)	19 (4.0)
Esomeprazole	7 (2.9)	7 (3.0)	14 (3.0)
Nexium	8 (3.3)	3 (1.3)	11 (2.3)
Famotidine	3 (1.3)	7 (3.0)	10 (2.1)
Lansoprazole	4 (1.7)	6 (2.6)	10 (2.1)
Pantoloc	7 (2.9)	2 (0.9)	9 (1.9)
Controloc	2 (0.8)	3 (1.3)	5 (1.1)
Omepradex	3 (1.3)	2 (0.9)	5 (1.1)
Pantoprazole Magnesium	3 (1.3)	1 (0.4)	4 (0.8)
Pantoprazolo	2 (0.8)	2 (0.9)	4 (0.8)
Losec	3 (1.3)	0	3 (0.6)
Pantip	2 (0.8)	1 (0.4)	3 (0.6)
Esomeprazolo	2 (0.8)	0	2 (0.4)
Lanzoprazole	1 (0.4)	1 (0.4)	2 (0.4)
Pantoprozole	2 (0.8)	0	2 (0.4)
Pirenzepin	0	2 (0.9)	2 (0.4)
Ranitidine	1 (0.4)	1 (0.4)	2 (0.4)
Zantac	2 (0.8)	0	2 (0.4)
Anagastra	0	1 (0.4)	1 (0.2)
Antiacid	1 (0.4)	0	1 (0.2)
Cimetidin	1 (0.4)	0	1 (0.2)
Dexilant	1 (0.4)	0	1 (0.2)
Enamera	1 (0.4)	0	1 (0.2)
Esmoprazole	0	1 (0.4)	1 (0.2)
Esomepraol	0	1 (0.4)	1 (0.2)
Esomepraozol	1 (0.4)	0	1 (0.2)
Esomeprazol Hemimagnesion	1 (0.4)	0	1 (0.2)
Esoprim S.K	1 (0.4)	0	1 (0.2)
Eupantol	1 (0.4)	0	1 (0.2)
Ezomeprazole	1 (0.4)	0	1 (0.2)
Famitodine	1 (0.4)	0	1 (0.2)
Famotidine (Gastro)	0	1 (0.4)	1 (0.2)
Gastro (Famotidine)	0	1 (0.4)	1 (0.2)
Inexium	1 (0.4)	0	1 (0.2)
Lansoprazol	1 (0.4)	0	1 (0.2)

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Lansoprazolo	0	1 (0.4)	1 (0.2)
Lanton	1 (0.4)	0	1 (0.2)
Lanton Cap	0	1 (0.4)	1 (0.2)
Lanzoprazolo	0	1 (0.4)	1 (0.2)
Nexiam	1 (0.4)	0	1 (0.2)
Nexium (Esomeprazol)	0	1 (0.4)	1 (0.2)
Nexium- Esomeprazole	1 (0.4)	0	1 (0.2)
Nolpaza	1 (0.4)	0	1 (0.2)
Omeoprazolo	1 (0.4)	0	1 (0.2)
Omeprasol	1 (0.4)	0	1 (0.2)
Omeprazol Syrup	0	1 (0.4)	1 (0.2)
Omeprazolo	1 (0.4)	0	1 (0.2)
Pantaprazole	1 (0.4)	0	1 (0.2)
Pantomed (Pantoprazol Natrium)	1 (0.4)	0	1 (0.2)
Pantomed (Pantoprazole Natrium)	1 (0.4)	0	1 (0.2)
Pantoprasol	0	1 (0.4)	1 (0.2)
Pantopraxol	1 (0.4)	0	1 (0.2)
Pantoprazol 40 Mg/100 Ml	0	1 (0.4)	1 (0.2)
Pantoprazol Al	1 (0.4)	0	1 (0.2)
Pantoprazol Natrium	0	1 (0.4)	1 (0.2)
Pantoprazolum	1 (0.4)	0	1 (0.2)
Pantoprozol	1 (0.4)	0	1 (0.2)
Pantroprazole	0	1 (0.4)	1 (0.2)
Prilosec Dr	0	1 (0.4)	1 (0.2)
Protonix	1 (0.4)	0	1 (0.2)
Ranitidine Hcl	0	1 (0.4)	1 (0.2)
Somac	1 (0.4)	0	1 (0.2)
Sulcrate	1 (0.4)	0	1 (0.2)
Naloxon	6 (2.5)	5 (2.2)	11 (2.3)
DRUGS USED IN ADDICTIVE DISORDERS	8 (3.3)	10 (4.3)	18 (3.8)
Nicotine	0	3 (1.3)	3 (0.6)
Nicorette	1 (0.4)	1 (0.4)	2 (0.4)
Buprenorphinum	1 (0.4)	0	1 (0.2)
Methadone	0	1 (0.4)	1 (0.2)
Nicotine Patch	1 (0.4)	0	1 (0.2)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY	37 (15.5)	24 (10.3)	61 (13.0)
Tamsulosin	15 (6.3)	10 (4.3)	25 (5.3)
Tamsulosine	2 (0.8)	4 (1.7)	6 (1.3)
Xatral	3 (1.3)	2 (0.9)	5 (1.1)
Finasteride	3 (1.3)	1 (0.4)	4 (0.8)
Tamsulosina	3 (1.3)	1 (0.4)	4 (0.8)
Dutasterid	3 (1.3)	0	3 (0.6)
Dutasteride	2 (0.8)	1 (0.4)	3 (0.6)
Alfuzosine	1 (0.4)	1 (0.4)	2 (0.4)
Dutasterida	1 (0.4)	1 (0.4)	2 (0.4)
Terazosin	1 (0.4)	1 (0.4)	2 (0.4)
Alfuzosin	1 (0.4)	0	1 (0.2)
Alfuzosine (Xatral) Lp 5 Mg	1 (0.4)	0	1 (0.2)
Avodart Cap 0.5 Mg	0	1 (0.4)	1 (0.2)
Doudart	1 (0.4)	0	1 (0.2)
Doxepin Neuroratiopharm	0	1 (0.4)	1 (0.2)
Duodart	1 (0.4)	0	1 (0.2)
Flomax	0	1 (0.4)	1 (0.2)

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Josir	1 (0.4)	0	1 (0.2)
Omnic	1 (0.4)	0	1 (0.2)
Permixon	0	1 (0.4)	1 (0.2)
Pygeum Africanum Extrait	1 (0.4)	0	1 (0.2)
Silodosina	0	1 (0.4)	1 (0.2)
Tamsulosin 400 Mcg	1 (0.4)	0	1 (0.2)
Tamsulosin Hcl	1 (0.4)	0	1 (0.2)
Tamsulosinhydrochlorid	1 (0.4)	0	1 (0.2)
Tamsulosinhydroklorid	1 (0.4)	0	1 (0.2)
Tamusulosin	0	1 (0.4)	1 (0.2)
Zoxazosin	1 (0.4)	0	1 (0.2)
EMOLLIENTS AND PROTECTIVES	2 (0.8)	4 (1.7)	6 (1.3)
Dexeryl	1 (0.4)	1 (0.4)	2 (0.4)
Avene Cicalfate	1 (0.4)	0	1 (0.2)
Cetomagrogolcreme	0	1 (0.4)	1 (0.2)
U10 Lipolotio	0	1 (0.4)	1 (0.2)
Vaseline	1 (0.4)	0	1 (0.2)
Vaseline/Paraffine	0	1 (0.4)	1 (0.2)
ESTROGENS	3 (1.3)	1 (0.4)	4 (0.8)
Estriol	1 (0.4)	1 (0.4)	2 (0.4)
Estreva	1 (0.4)	0	1 (0.2)
Synapause	1 (0.4)	0	1 (0.2)
Natriumchlorid	1 (0.4)	0	1 (0.2)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS	16 (6.7)	15 (6.5)	31 (6.6)
Acetylcystein	2 (0.8)	5 (2.2)	7 (1.5)
Acetylcysteine	3 (1.3)	3 (1.3)	6 (1.3)
Guaifenesin	2 (0.8)	2 (0.9)	4 (0.8)
Nacl	4 (1.7)	0	4 (0.8)
Acc	3 (1.3)	0	3 (0.6)
Acetilcisteina	0	1 (0.4)	1 (0.2)
Acetylcysteine 20%	1 (0.4)	0	1 (0.2)
Ambroxol	0	1 (0.4)	1 (0.2)
Fluimicil	1 (0.4)	0	1 (0.2)
Mucoclear	0	1 (0.4)	1 (0.2)
Natriumchloride	1 (0.4)	0	1 (0.2)
Reolin	0	1 (0.4)	1 (0.2)
Sodium Chloride 3%	1 (0.4)	0	1 (0.2)
Sodium_chloride 3%	0	1 (0.4)	1 (0.2)
HEMODIALYTICS AND HEMOFILTRATES	3 (1.3)	0	3 (0.6)
Elo Mel	1 (0.4)	0	1 (0.2)
Kalium	1 (0.4)	0	1 (0.2)
Ringer-Acetat	1 (0.4)	0	1 (0.2)
HERBAL ANTIBACTERIALS AND ANTIINFECTIVES FOR SYSTEMIC USE	1 (0.4)	0	1 (0.2)
Femannose	1 (0.4)	0	1 (0.2)
HIGH-CEILING DIURETICS	113 (47.3)	106 (45.7)	219 (46.5)
Furosemide	46 (19.2)	43 (18.5)	89 (18.9)
Torasemid	35 (14.6)	28 (12.1)	63 (13.4)
Furosemid	27 (11.3)	25 (10.8)	52 (11.0)
Lasix	9 (3.8)	2 (0.9)	11 (2.3)

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Fusid	2 (0.8)	4 (1.7)	6 (1.3)
Burinex	2 (0.8)	3 (1.3)	5 (1.1)
Torasemide	3 (1.3)	2 (0.9)	5 (1.1)
Torem	1 (0.4)	4 (1.7)	5 (1.1)
Bumetanide	1 (0.4)	2 (0.9)	3 (0.6)
Furon	2 (0.8)	0	2 (0.4)
Furosemida	0	2 (0.9)	2 (0.4)
Furosã©mide	1 (0.4)	1 (0.4)	2 (0.4)
Bumetamide	0	1 (0.4)	1 (0.2)
Forusemide	1 (0.4)	0	1 (0.2)
Furosemid / Furosemide	1 (0.4)	0	1 (0.2)
Furosemide 20mg/2ml	0	1 (0.4)	1 (0.2)
Furosemidi	1 (0.4)	0	1 (0.2)
Furosemidum	1 (0.4)	0	1 (0.2)
Furosimide	1 (0.4)	0	1 (0.2)
Fusid- Furosemide	1 (0.4)	0	1 (0.2)
Lasilix	0	1 (0.4)	1 (0.2)
Lasix/Furosemid	1 (0.4)	0	1 (0.2)
Seguril	1 (0.4)	0	1 (0.2)
Toramide/Torasemide	1 (0.4)	0	1 (0.2)
Torasemidum	1 (0.4)	0	1 (0.2)
Torsemide	0	1 (0.4)	1 (0.2)
Cadex	1 (0.4)	0	1 (0.2)
HORMONE ANTAGONISTS AND RELATED AGENTS	5 (2.1)	2 (0.9)	7 (1.5)
Letrozol	2 (0.8)	0	2 (0.4)
Anastrozol	1 (0.4)	0	1 (0.2)
Bicalutamid	0	1 (0.4)	1 (0.2)
Exomestane 25mg, Tablet	1 (0.4)	0	1 (0.2)
Letrozole	0	1 (0.4)	1 (0.2)
Midazolam	15 (6.3)	13 (5.6)	28 (5.9)
Promethazine	1 (0.4)	0	1 (0.2)
HYPNOTICS AND SEDATIVES	74 (31.0)	64 (27.6)	138 (29.3)
Melatonin	22 (9.2)	25 (10.8)	47 (10.0)
Zolpidem	2 (0.8)	6 (2.6)	8 (1.7)
Zopiclon	5 (2.1)	3 (1.3)	8 (1.7)
Circadin	5 (2.1)	2 (0.9)	7 (1.5)
Zopiclone	2 (0.8)	5 (2.2)	7 (1.5)
Dexdor	0	3 (1.3)	3 (0.6)
Dexmedetomidine	0	3 (1.3)	3 (0.6)
Imovane	3 (1.3)	0	3 (0.6)
Temazepam	3 (1.3)	0	3 (0.6)
Zoldem	3 (1.3)	0	3 (0.6)
Dexmedetomidin	1 (0.4)	1 (0.4)	2 (0.4)
Dormicum	1 (0.4)	1 (0.4)	2 (0.4)
Halcion	2 (0.8)	0	2 (0.4)
Lormetazepam	1 (0.4)	1 (0.4)	2 (0.4)
Melatonine	0	2 (0.9)	2 (0.4)
Sedistress	1 (0.4)	1 (0.4)	2 (0.4)
Stilnox	2 (0.8)	0	2 (0.4)
Valerian	1 (0.4)	1 (0.4)	2 (0.4)
Bondormin	1 (0.4)	0	1 (0.2)
Bondromin	1 (0.4)	0	1 (0.2)
Brotizolam	1 (0.4)	0	1 (0.2)

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Chloralhydrat	0	1 (0.4)	1 (0.2)
Clomethiazole	1 (0.4)	0	1 (0.2)
Deksmedetomidin	1 (0.4)	0	1 (0.2)
Dexamedetomidin	1 (0.4)	0	1 (0.2)
Dexamedetomidine	0	1 (0.4)	1 (0.2)
Dexamedetomidine Hcl	1 (0.4)	0	1 (0.2)
Dexmedetomidine Inet Premix	1 (0.4)	0	1 (0.2)
Dexmedetomidine Sodium Chloride	0	1 (0.4)	1 (0.2)
Dexmedetotomidin	0	1 (0.4)	1 (0.2)
Dexmetomidine	0	1 (0.4)	1 (0.2)
Diphenyramine	1 (0.4)	0	1 (0.2)
Dormicum 5 Mg	1 (0.4)	0	1 (0.2)
Doxepin	1 (0.4)	0	1 (0.2)
Estazolam	1 (0.4)	0	1 (0.2)
Hypnovel	1 (0.4)	0	1 (0.2)
Lendorm	0	1 (0.4)	1 (0.2)
Midazol	0	1 (0.4)	1 (0.2)
Midazolame	0	1 (0.4)	1 (0.2)
Noctamid	1 (0.4)	0	1 (0.2)
Precedex	0	1 (0.4)	1 (0.2)
Promethzine	1 (0.4)	0	1 (0.2)
Scopoderm	1 (0.4)	0	1 (0.2)
Ximovan	1 (0.4)	0	1 (0.2)
Zopiklone	1 (0.4)	0	1 (0.2)
Nacl	1 (0.4)	1 (0.4)	2 (0.4)
Kalium	0	3 (1.3)	3 (0.6)
I.V. SOLUTION ADDITIVES	44 (18.4)	45 (19.4)	89 (18.9)
Potassium Chloride	7 (2.9)	8 (3.4)	15 (3.2)
Kaliumchlorid	4 (1.7)	8 (3.4)	12 (2.5)
Potassium Phosphate	4 (1.7)	3 (1.3)	7 (1.5)
Kcl	4 (1.7)	2 (0.9)	6 (1.3)
Kaliumchloride	2 (0.8)	3 (1.3)	5 (1.1)
Magnesium Sulfate	2 (0.8)	2 (0.9)	4 (0.8)
Magnesiumsulfat	3 (1.3)	1 (0.4)	4 (0.8)
Sodium Phosphate	1 (0.4)	3 (1.3)	4 (0.8)
Normal Saline	2 (0.8)	1 (0.4)	3 (0.6)
Potassium	1 (0.4)	2 (0.9)	3 (0.6)
Sodium Chloride	1 (0.4)	2 (0.9)	3 (0.6)
Addaven	2 (0.8)	0	2 (0.4)
Calcium Gluconate	0	2 (0.9)	2 (0.4)
Magnesium Sulphate	0	2 (0.9)	2 (0.4)
Sodio Cloruro	0	2 (0.9)	2 (0.4)
0.9% Nacl	0	1 (0.4)	1 (0.2)
3% Nacl	1 (0.4)	0	1 (0.2)
3% Sodium Chloride	0	1 (0.4)	1 (0.2)
Calcium Gluconat	1 (0.4)	0	1 (0.2)
Cemevit	1 (0.4)	0	1 (0.2)
Cernevit	0	1 (0.4)	1 (0.2)
Electrolyte-A Iv Solution 1,000 Ml	0	1 (0.4)	1 (0.2)
Electrolytes (3 G Kcl, 2 G Mgso4, 6 Iu Insulin, 5 Ml Lidocaine 2% And 500 Ml 5% Glucose)	1 (0.4)	0	1 (0.2)
Glycerol Dihydrogenphosphat	1 (0.4)	0	1 (0.2)
Halbisotone Nacl	1 (0.4)	0	1 (0.2)
Kalii Phosphate	1 (0.4)	0	1 (0.2)
Kalium Chloratum 7.5%	1 (0.4)	0	1 (0.2)

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Kaliumchlorid 7,46%	1 (0.4)	0	1 (0.2)
Kaliumchlorid 7.46%	1 (0.4)	0	1 (0.2)
Kaliumcloride	1 (0.4)	0	1 (0.2)
Kaliumhydrochloride	1 (0.4)	0	1 (0.2)
Kaliumhydrogenfosfat	1 (0.4)	0	1 (0.2)
Magesium Sulfate	0	1 (0.4)	1 (0.2)
Magnesium	1 (0.4)	0	1 (0.2)
Magnesium Sulfaat	1 (0.4)	0	1 (0.2)
Magnesium Sulfate 1 G In Dextrose 5% 100 Ml Premix Ivpb	0	1 (0.4)	1 (0.2)
Magnesium Sulfate 4 G In Sterile Water 50 Ml Premix Ivpb	0	1 (0.4)	1 (0.2)
Magnesiumsulphate	1 (0.4)	0	1 (0.2)
Magnesuim Sulfate	1 (0.4)	0	1 (0.2)
N/S 0.9%	1 (0.4)	0	1 (0.2)
Nacl 0.9%	0	1 (0.4)	1 (0.2)
Natrium Chloratum 0.9%	1 (0.4)	0	1 (0.2)
Natriumbicarbonat	0	1 (0.4)	1 (0.2)
Natriumchloride Isoton	1 (0.4)	0	1 (0.2)
Normal Saline Bolus	0	1 (0.4)	1 (0.2)
Potasion	1 (0.4)	0	1 (0.2)
Potassium Chlorid	0	1 (0.4)	1 (0.2)
Potassium Chloride 1 Molar	1 (0.4)	0	1 (0.2)
Potassium Chlorure	0	1 (0.4)	1 (0.2)
Potassium Chlorure 15%, Perfusion	1 (0.4)	0	1 (0.2)
Potassiumchloride Fluids	1 (0.4)	0	1 (0.2)
Saline Solution Physiological	0	1 (0.4)	1 (0.2)
Sodium Chloride (Nacl 0.45%)	1 (0.4)	0	1 (0.2)
Sodium Chloride 0.9% Bolus 750ml	1 (0.4)	0	1 (0.2)
Sodium Chloride 3% Premix Iv (Bolus)	0	1 (0.4)	1 (0.2)
Sodium Chloride 4 Meq/Ml	0	1 (0.4)	1 (0.2)
Sodium Chloride 4 Meq/Ml Injection	0	1 (0.4)	1 (0.2)
Sodium Chloride Solution	1 (0.4)	0	1 (0.2)
Soluvit	1 (0.4)	0	1 (0.2)
Sulfate Magnã©sium	1 (0.4)	0	1 (0.2)
Trometamol	1 (0.4)	0	1 (0.2)
Vitalipid	1 (0.4)	0	1 (0.2)
Zinc	0	1 (0.4)	1 (0.2)
I.V. SOLUTIONS	30 (12.6)	28 (12.1)	58 (12.3)
Mannitol	7 (2.9)	4 (1.7)	11 (2.3)
Glucose	5 (2.1)	0	5 (1.1)
Elomel Isoton	1 (0.4)	2 (0.9)	3 (0.6)
Jonosteril	1 (0.4)	2 (0.9)	3 (0.6)
Manitol	1 (0.4)	2 (0.9)	3 (0.6)
Mannitol 20%	1 (0.4)	2 (0.9)	3 (0.6)
Elo Iso Isoton	1 (0.4)	1 (0.4)	2 (0.4)
Elomel	2 (0.8)	0	2 (0.4)
Elozell	1 (0.4)	1 (0.4)	2 (0.4)
Glucose 5%	0	2 (0.9)	2 (0.4)
Kabiven Perifer	1 (0.4)	1 (0.4)	2 (0.4)
Mannitolo	0	2 (0.9)	2 (0.4)
Plasmalyte	1 (0.4)	1 (0.4)	2 (0.4)
5% Dextrose	0	1 (0.4)	1 (0.2)
Aminoven	1 (0.4)	0	1 (0.2)
Dextro Energy	1 (0.4)	0	1 (0.2)
Elo-Mel	0	1 (0.4)	1 (0.2)

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Fluids 5% Glucose	1 (0.4)	0	1 (0.2)
Glucose 10%	0	1 (0.4)	1 (0.2)
Glucose 10% Discontinu	1 (0.4)	0	1 (0.2)
Glucose B.Braun 50 Mg/Ml - Inf-Lsg	0	1 (0.4)	1 (0.2)
Glucose Solution	1 (0.4)	0	1 (0.2)
Inzolen	1 (0.4)	0	1 (0.2)
Lactated Ringer's	0	1 (0.4)	1 (0.2)
Lactated Ringers	1 (0.4)	0	1 (0.2)
Lipofundin	1 (0.4)	0	1 (0.2)
Manitol 20%	1 (0.4)	0	1 (0.2)
Mannitol 20% Premix Iv	0	1 (0.4)	1 (0.2)
Mannitole 18%	0	1 (0.4)	1 (0.2)
Mannitole 20%	0	1 (0.4)	1 (0.2)
Nurtriflex	0	1 (0.4)	1 (0.2)
Nutriflex Lipid Peri B. Braun - Emulsion Zur Infusion	0	1 (0.4)	1 (0.2)
Optilyte/Electrolites	1 (0.4)	0	1 (0.2)
Parenteral Nutrition Olimer Perifer N4e	1 (0.4)	0	1 (0.2)
Periolimel	1 (0.4)	0	1 (0.2)
Plasmalyte A	0	1 (0.4)	1 (0.2)
Polyionique	1 (0.4)	0	1 (0.2)
Ringer-Lactat	0	1 (0.4)	1 (0.2)
Smofkabiven	0	1 (0.4)	1 (0.2)
Smofkabiven Zentral - Emulsion Zur Infusion	0	1 (0.4)	1 (0.2)
Sodium Chloride 3% Bolus	0	1 (0.4)	1 (0.2)
Sterofundin	1 (0.4)	0	1 (0.2)
Sterofundine	0	1 (0.4)	1 (0.2)
IMMUNOSUPPRESSANTS	4 (1.7)	6 (2.6)	10 (2.1)
Leflunomide	0	3 (1.3)	3 (0.6)
Tacrolimus	2 (0.8)	1 (0.4)	3 (0.6)
Leflunomid	1 (0.4)	0	1 (0.2)
Lefunamid	0	1 (0.4)	1 (0.2)
Mycofenolaat	1 (0.4)	0	1 (0.2)
Mycophenacid	1 (0.4)	0	1 (0.2)
Mycophenolate	1 (0.4)	0	1 (0.2)
Prograf	0	1 (0.4)	1 (0.2)
INSULINS AND ANALOGUES	53 (22.2)	43 (18.5)	96 (20.4)
Insulin	10 (4.2)	6 (2.6)	16 (3.4)
Novorapid	6 (2.5)	5 (2.2)	11 (2.3)
Insulin Glargine	5 (2.1)	3 (1.3)	8 (1.7)
Insuline	7 (2.9)	1 (0.4)	8 (1.7)
Rapid Insuline	1 (0.4)	6 (2.6)	7 (1.5)
Actrapid	4 (1.7)	2 (0.9)	6 (1.3)
Lantus	4 (1.7)	1 (0.4)	5 (1.1)
Insulin Lantus	1 (0.4)	3 (1.3)	4 (0.8)
Insulin Lispro	3 (1.3)	1 (0.4)	4 (0.8)
Humalog	1 (0.4)	2 (0.9)	3 (0.6)
Insulin Aspart	2 (0.8)	1 (0.4)	3 (0.6)
Insulin Regular	1 (0.4)	2 (0.9)	3 (0.6)
Abasaglar	1 (0.4)	1 (0.4)	2 (0.4)
Glargine Insuline	0	2 (0.9)	2 (0.4)
Huminsulin	0	2 (0.9)	2 (0.4)
Insulatard	0	2 (0.9)	2 (0.4)
Insulin Correction	1 (0.4)	1 (0.4)	2 (0.4)

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Insuman Rapid	0	2 (0.9)	2 (0.4)
Lantus Insuline	1 (0.4)	1 (0.4)	2 (0.4)
Toujeo	2 (0.8)	0	2 (0.4)
Actraphane	1 (0.4)	0	1 (0.2)
Actrapid Insulin	1 (0.4)	0	1 (0.2)
Basaglar	1 (0.4)	0	1 (0.2)
Fiasp Insuline	0	1 (0.4)	1 (0.2)
Gensulin R	1 (0.4)	0	1 (0.2)
Glargine	0	1 (0.4)	1 (0.2)
H-Insulin	0	1 (0.4)	1 (0.2)
Humalog Insulin	0	1 (0.4)	1 (0.2)
Humalog Rapid	1 (0.4)	0	1 (0.2)
Humaninsulin	0	1 (0.4)	1 (0.2)
Humulin R	0	1 (0.4)	1 (0.2)
Insuilin Correction	0	1 (0.4)	1 (0.2)
Insulin Humulin N	1 (0.4)	0	1 (0.2)
Insulin Humulin R	1 (0.4)	0	1 (0.2)
Insulin Humulin R Sliding Scale	1 (0.4)	0	1 (0.2)
Insulin (Novorapid)	0	1 (0.4)	1 (0.2)
Insulin Actrapid	1 (0.4)	0	1 (0.2)
Insulin Apira Solostar	0	1 (0.4)	1 (0.2)
Insulin Aspart (Novorapid Penfill)	0	1 (0.4)	1 (0.2)
Insulin Aspart (Novorapid Plex Pen)	0	1 (0.4)	1 (0.2)
Insulin Aspart:	1 (0.4)	0	1 (0.2)
Insulin Detemir	1 (0.4)	0	1 (0.2)
Insulin Glargin	1 (0.4)	0	1 (0.2)
Insulin Glargine (Insulin Lantus)	0	1 (0.4)	1 (0.2)
Insulin Grargine	0	1 (0.4)	1 (0.2)
Insulin Humalog- Reduced S/S	1 (0.4)	0	1 (0.2)
Insulin Mixtard 30	1 (0.4)	0	1 (0.2)
Insulin Novorapid	1 (0.4)	0	1 (0.2)
Insulin Novorapid Plex Pen	0	1 (0.4)	1 (0.2)
Insulin Reg Sliding Scale	0	1 (0.4)	1 (0.2)
Insulin-Alt	1 (0.4)	0	1 (0.2)
Insulin-Lispro	1 (0.4)	0	1 (0.2)
Insulina Lispro	0	1 (0.4)	1 (0.2)
Insuline Asparte	0	1 (0.4)	1 (0.2)
Insuline Dã©tã©mir (Levemir) 100ui/Ml	1 (0.4)	0	1 (0.2)
Insuline Humaine (Umuline Rapide)	1 (0.4)	0	1 (0.2)
Insuline Insuman Rapid	1 (0.4)	0	1 (0.2)
Insuline Lantus	1 (0.4)	0	1 (0.2)
Insuline Lispro (Humalog) 100ui/Ml	1 (0.4)	0	1 (0.2)
Insuline Novorapid Flexpen	1 (0.4)	0	1 (0.2)
Insuline Rapid	0	1 (0.4)	1 (0.2)
Insuline-Glargine Long Action 100u/Ml	1 (0.4)	0	1 (0.2)
Insulun Basaglar Crt	0	1 (0.4)	1 (0.2)
Insuman Comb	1 (0.4)	0	1 (0.2)
Isophaninsulin (Human)	1 (0.4)	0	1 (0.2)
Lastus Insuline	0	1 (0.4)	1 (0.2)
Levemir	1 (0.4)	0	1 (0.2)
Novarapid	0	1 (0.4)	1 (0.2)
Novomix	1 (0.4)	0	1 (0.2)
Novopraid	0	1 (0.4)	1 (0.2)
Rapid Acting Insuline	1 (0.4)	0	1 (0.2)
Short Acting Insulin	1 (0.4)	0	1 (0.2)

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Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Toujeo Insulin	0	1 (0.4)	1 (0.2)
INTESTINAL ADSORBENTS	1 (0.4)	0	1 (0.2)
Diosmectite 3g, Sachet	1 (0.4)	0	1 (0.2)
INTESTINAL ANTIINFECTIVES	1 (0.4)	3 (1.3)	4 (0.8)
Amphotericine B	0	3 (1.3)	3 (0.6)
Fidaxomicin	1 (0.4)	0	1 (0.2)
Budesonide	1 (0.4)	1 (0.4)	2 (0.4)
INTESTINAL ANTIINFLAMMATORY AGENTS	1 (0.4)	1 (0.4)	2 (0.4)
Mesalazine	0	1 (0.4)	1 (0.2)
IODINE THERAPY	1 (0.4)	1 (0.4)	2 (0.4)
Iodid-Ion	0	1 (0.4)	1 (0.2)
Kaliumiodid	1 (0.4)	0	1 (0.2)
IRON PREPARATIONS	13 (5.4)	4 (1.7)	17 (3.6)
Ferrous Sulfate	2 (0.8)	1 (0.4)	3 (0.6)
Ferro Sanol	2 (0.8)	0	2 (0.4)
Ferrous Fumarate	1 (0.4)	1 (0.4)	2 (0.4)
Ferbisol	1 (0.4)	0	1 (0.2)
Ferrifol	1 (0.4)	0	1 (0.2)
Ferrodyn	1 (0.4)	0	1 (0.2)
Ferrofumaraat	0	1 (0.4)	1 (0.2)
Ferrofumerate	1 (0.4)	0	1 (0.2)
Ferrosanol	1 (0.4)	0	1 (0.2)
Ferrosulphate	1 (0.4)	0	1 (0.2)
Iron C	1 (0.4)	0	1 (0.2)
Ironglycinsulfat	1 (0.4)	0	1 (0.2)
Maltofer	1 (0.4)	0	1 (0.2)
Neoferrofolgamma	0	1 (0.4)	1 (0.2)
IRRIGATING SOLUTIONS	2 (0.8)	2 (0.9)	4 (0.8)
Natriumhydrogencarbonat	1 (0.4)	2 (0.9)	3 (0.6)
Physiological Serum	1 (0.4)	0	1 (0.2)
LIPID MODIFYING AGENTS, COMBINATIONS	3 (1.3)	1 (0.4)	4 (0.8)
Ezetimibe+ Simvastatina	1 (0.4)	0	1 (0.2)
Ezetimibe/Rosuvastatin	1 (0.4)	0	1 (0.2)
Inegy	1 (0.4)	0	1 (0.2)
Suvezen	0	1 (0.4)	1 (0.2)
LIPID MODIFYING AGENTS, PLAIN	122 (51.0)	113 (48.7)	235 (49.9)
Atorvastatin	47 (19.7)	44 (19.0)	91 (19.3)
Simvastatin	23 (9.6)	19 (8.2)	42 (8.9)
Rosuvastatin	15 (6.3)	9 (3.9)	24 (5.1)
Atorvastatine	6 (2.5)	9 (3.9)	15 (3.2)
Ezetimibe	4 (1.7)	4 (1.7)	8 (1.7)
Lipitor	2 (0.8)	6 (2.6)	8 (1.7)
Simvastatine	1 (0.4)	7 (3.0)	8 (1.7)
Atrovastatin	4 (1.7)	3 (1.3)	7 (1.5)
Rosuvastatine	4 (1.7)	3 (1.3)	7 (1.5)
Crestor	5 (2.1)	1 (0.4)	6 (1.3)
Ezetimib	3 (1.3)	1 (0.4)	4 (0.8)

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Pravastatin	2 (0.8)	2 (0.9)	4 (0.8)
Atorvastatina	1 (0.4)	2 (0.9)	3 (0.6)
Tahor	2 (0.8)	1 (0.4)	3 (0.6)
Atrovastatine	1 (0.4)	1 (0.4)	2 (0.4)
Fluvastatin	1 (0.4)	1 (0.4)	2 (0.4)
Simvacor	0	2 (0.9)	2 (0.4)
Sortis	1 (0.4)	1 (0.4)	2 (0.4)
Atoravastatine	0	1 (0.4)	1 (0.2)
Atorvastain	1 (0.4)	0	1 (0.2)
Atorvastatin 80mg	1 (0.4)	0	1 (0.2)
Atorvastatin Calcium	0	1 (0.4)	1 (0.2)
Atorvasterol / Atorvastatin	1 (0.4)	0	1 (0.2)
Atrovastatine Calcium	1 (0.4)	0	1 (0.2)
Bezofibrat	0	1 (0.4)	1 (0.2)
Crestastatin	0	1 (0.4)	1 (0.2)
Crestor (Rosuvastatine) 5 Mg	1 (0.4)	0	1 (0.2)
Ezetrol	0	1 (0.4)	1 (0.2)
Fenofibrate	1 (0.4)	0	1 (0.2)
Gemfibrozil	1 (0.4)	0	1 (0.2)
Gemfibrozilo	1 (0.4)	0	1 (0.2)
Litorva	0	1 (0.4)	1 (0.2)
Litorva- Atorvastatin	1 (0.4)	0	1 (0.2)
Omega 3-6-9 Complex	0	1 (0.4)	1 (0.2)
Pravastatina	0	1 (0.4)	1 (0.2)
Pravastatine	1 (0.4)	0	1 (0.2)
Romazic / Rosuvastatin	1 (0.4)	0	1 (0.2)
Rosuvastatin Calcium	0	1 (0.4)	1 (0.2)
Rosuvastatina	1 (0.4)	0	1 (0.2)
Rosuvastatine Teva	1 (0.4)	0	1 (0.2)
Rosvastatin	0	1 (0.4)	1 (0.2)
Selectin	0	1 (0.4)	1 (0.2)
Simvahexal	1 (0.4)	0	1 (0.2)
Simvastatina	0	1 (0.4)	1 (0.2)
Simvaxon	1 (0.4)	0	1 (0.2)
Wild Alaskan Salmon Oil	1 (0.4)	0	1 (0.2)
LOW-CEILING DIURETICS, EXCL. THIAZIDES	16 (6.7)	23 (9.9)	39 (8.3)
Indapamid	7 (2.9)	8 (3.4)	15 (3.2)
Indapamide	2 (0.8)	4 (1.7)	6 (1.3)
Xipamid	2 (0.8)	3 (1.3)	5 (1.1)
Chlorthalidone	1 (0.4)	3 (1.3)	4 (0.8)
Chlortalidon	0	2 (0.9)	2 (0.4)
Chlortalidone	1 (0.4)	1 (0.4)	2 (0.4)
Diamox	1 (0.4)	0	1 (0.2)
Hygroton / Chlortalidon	0	1 (0.4)	1 (0.2)
Indapamid Retard	1 (0.4)	0	1 (0.2)
Indapen	1 (0.4)	0	1 (0.2)
Pamid Tab 150	0	1 (0.4)	1 (0.2)
LOW-CEILING DIURETICS, THIAZIDES	41 (17.2)	26 (11.2)	67 (14.2)
Hydrochlorothiazid	10 (4.2)	11 (4.7)	21 (4.5)
Hydrochlorothiazide	10 (4.2)	4 (1.7)	14 (3.0)
Hct	3 (1.3)	3 (1.3)	6 (1.3)
Esidrex	2 (0.8)	1 (0.4)	3 (0.6)
Hydrochloorthiazide	2 (0.8)	1 (0.4)	3 (0.6)

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Hydrochlorthiazid	3 (1.3)	0	3 (0.6)
Disothiazide	2 (0.8)	0	2 (0.4)
Hydrochlorthiazide	2 (0.8)	0	2 (0.4)
Idroclorotiazide	1 (0.4)	1 (0.4)	2 (0.4)
Chlorothiazide	1 (0.4)	0	1 (0.2)
Disothiazide (Hydrichlorothiazide)	1 (0.4)	0	1 (0.2)
Hct Hydrochlorothiazid	1 (0.4)	0	1 (0.2)
Hidroclorotiazide	0	1 (0.4)	1 (0.2)
Hydrochloro Thiazide	1 (0.4)	0	1 (0.2)
Hydrochlorothiacid	0	1 (0.4)	1 (0.2)
Hydrochlorothiaz	0	1 (0.4)	1 (0.2)
Hydrochlorothiazid Hct	1 (0.4)	0	1 (0.2)
Hydrochlorotiazid	0	1 (0.4)	1 (0.2)
Hydrocholorothiazid	0	1 (0.4)	1 (0.2)
Hydroclorotiazida	1 (0.4)	0	1 (0.2)
Hydroclorotiazide	1 (0.4)	0	1 (0.2)
MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS	13 (5.4)	12 (5.2)	25 (5.3)
Clindamycin	2 (0.8)	4 (1.7)	6 (1.3)
Erythromycin	3 (1.3)	2 (0.9)	5 (1.1)
Clarithromycin	4 (1.7)	0	4 (0.8)
Azithromycin	1 (0.4)	1 (0.4)	2 (0.4)
Aziatromicina	0	1 (0.4)	1 (0.2)
Azitromicina	1 (0.4)	0	1 (0.2)
Azitromycin	0	1 (0.4)	1 (0.2)
Azythromicin	0	1 (0.4)	1 (0.2)
Clarithromicin	0	1 (0.4)	1 (0.2)
Claritromicina	1 (0.4)	0	1 (0.2)
Clindamicyn	0	1 (0.4)	1 (0.2)
Clindamycin 100	1 (0.4)	0	1 (0.2)
Clindamycine	1 (0.4)	0	1 (0.2)
Eritromicine	0	1 (0.4)	1 (0.2)
MAGNETIC RESONANCE IMAGING CONTRAST MEDIA	0	1 (0.4)	1 (0.2)
Gadoterate Meglumine	0	1 (0.4)	1 (0.2)
MULTIVITAMINS, COMBINATIONS	1 (0.4)	0	1 (0.2)
Centrum Forte	1 (0.4)	0	1 (0.2)
MUSCLE RELAXANTS, CENTRALLY ACTING AGENTS	7 (2.9)	4 (1.7)	11 (2.3)
Baclofen	2 (0.8)	3 (1.3)	5 (1.1)
Baclofene	1 (0.4)	1 (0.4)	2 (0.4)
Cyclobenzaprine	1 (0.4)	0	1 (0.2)
Methocarbamol	1 (0.4)	0	1 (0.2)
Mydocalm / Tolperisone	1 (0.4)	0	1 (0.2)
Neodolpasse	1 (0.4)	0	1 (0.2)
Tizanidine	1 (0.4)	0	1 (0.2)
MUSCLE RELAXANTS, PERIPHERALLY ACTING AGENTS	9 (3.8)	12 (5.2)	21 (4.5)
Rocuronium	6 (2.5)	6 (2.6)	12 (2.5)
Esmeron	1 (0.4)	2 (0.9)	3 (0.6)
Vecuronium	1 (0.4)	1 (0.4)	2 (0.4)
Cisatracurium	0	1 (0.4)	1 (0.2)
Esmerone	0	1 (0.4)	1 (0.2)
Imeron 350	0	1 (0.4)	1 (0.2)

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Rocubronium	0	1 (0.4)	1 (0.2)
Rocuronium Bromide	1 (0.4)	0	1 (0.2)
Rocuroniumbromid	1 (0.4)	0	1 (0.2)
Fentanyl	6 (2.5)	4 (1.7)	10 (2.1)
OPIOIDS	84 (35.1)	76 (32.8)	160 (34.0)
Morphine	13 (5.4)	18 (7.8)	31 (6.6)
Piritramid	21 (8.8)	9 (3.9)	30 (6.4)
Morphin	16 (6.7)	12 (5.2)	28 (5.9)
Tramadol	7 (2.9)	9 (3.9)	16 (3.4)
Hydromorphone	7 (2.9)	7 (3.0)	14 (3.0)
Oxycodone	9 (3.8)	2 (0.9)	11 (2.3)
Morfine	4 (1.7)	3 (1.3)	7 (1.5)
Dipidolor	3 (1.3)	3 (1.3)	6 (1.3)
Tilidin	3 (1.3)	2 (0.9)	5 (1.1)
Oxycodon	1 (0.4)	3 (1.3)	4 (0.8)
Morfin	3 (1.3)	0	3 (0.6)
Piritramide	0	3 (1.3)	3 (0.6)
Buprenorphine	2 (0.8)	0	2 (0.4)
Hydromorphon	2 (0.8)	0	2 (0.4)
Morphini Sulfas	2 (0.8)	0	2 (0.4)
Oramorph	1 (0.4)	1 (0.4)	2 (0.4)
Oxycontin	1 (0.4)	1 (0.4)	2 (0.4)
Tradonal	1 (0.4)	1 (0.4)	2 (0.4)
Vendal	0	2 (0.9)	2 (0.4)
Vendal (Morphin Hydrochlorid Trihydrat)	2 (0.8)	0	2 (0.4)
Zamudol	1 (0.4)	1 (0.4)	2 (0.4)
Contramal	0	1 (0.4)	1 (0.2)
Durogesic	1 (0.4)	0	1 (0.2)
Fenta 12.5 Mcg/H	0	1 (0.4)	1 (0.2)
Fentanyl (Fenta 12.5 Mcg/H)	0	1 (0.4)	1 (0.2)
Frntanyl (Fenta 12.5 Mcg/H)	0	1 (0.4)	1 (0.2)
Hydal	1 (0.4)	0	1 (0.2)
Hydrocodene Acetaminophen	0	1 (0.4)	1 (0.2)
Hydromorphine	1 (0.4)	0	1 (0.2)
Morfina	1 (0.4)	0	1 (0.2)
Morphic	1 (0.4)	0	1 (0.2)
Morphic Chloride	0	1 (0.4)	1 (0.2)
Morphin Hydrochlorid Trihydrat	0	1 (0.4)	1 (0.2)
Morphin Perfusor	1 (0.4)	0	1 (0.2)
Morphin Retard	0	1 (0.4)	1 (0.2)
Morphine Chlorhidrate	1 (0.4)	0	1 (0.2)
Morphine Chlorydrate	0	1 (0.4)	1 (0.2)
Morphine Hcl	0	1 (0.4)	1 (0.2)
Morphine Hydrochloride	1 (0.4)	0	1 (0.2)
Morphine Sulfate	1 (0.4)	0	1 (0.2)
Morphine Sulphate	1 (0.4)	0	1 (0.2)
Norspan (Buprenorphine)	0	1 (0.4)	1 (0.2)
Oxanest	1 (0.4)	0	1 (0.2)
Oxycodone 5mg, Tablet	1 (0.4)	0	1 (0.2)
Oxycodone 5mg/2.5mg	1 (0.4)	0	1 (0.2)
Oxycodone Acetaminophen	0	1 (0.4)	1 (0.2)
Oxycodone Hydrochloride	1 (0.4)	0	1 (0.2)
Oxycodone/Acetaminophen	0	1 (0.4)	1 (0.2)
Oxygesic	0	1 (0.4)	1 (0.2)

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Oxylan Depot	1 (0.4)	0	1 (0.2)
Oxynorm	1 (0.4)	0	1 (0.2)
Percocet	0	1 (0.4)	1 (0.2)
Piriptramid	0	1 (0.4)	1 (0.2)
Piritramid / Dipidolor	1 (0.4)	0	1 (0.2)
Piritramiel Hamel	0	1 (0.4)	1 (0.2)
Pritramid	1 (0.4)	0	1 (0.2)
Rokacet Plus	0	1 (0.4)	1 (0.2)
Targin	1 (0.4)	0	1 (0.2)
Tilidin/Naloxan	0	1 (0.4)	1 (0.2)
Tilidin/Naloxon Retard	0	1 (0.4)	1 (0.2)
Topalgic	1 (0.4)	0	1 (0.2)
Tradonal Odis	0	1 (0.4)	1 (0.2)
Tramabene Retard	1 (0.4)	0	1 (0.2)
Tramadol Hci	0	1 (0.4)	1 (0.2)
Tramadol Hcl	0	1 (0.4)	1 (0.2)
Tramadol Zamudol	0	1 (0.4)	1 (0.2)
Tramal	0	1 (0.4)	1 (0.2)
Tramal Long	1 (0.4)	0	1 (0.2)
Tylenol	0	1 (0.4)	1 (0.2)
3			
Valtran	1 (0.4)	0	1 (0.2)
Natriumhydrogencarbonat	3 (1.3)	0	3 (0.6)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	3 (1.3)	2 (0.9)	5 (1.1)
Methionin	0	1 (0.4)	1 (0.2)
Prebiotic Fiber	0	1 (0.4)	1 (0.2)
Duloxetin	1 (0.4)	0	1 (0.2)
Pregabalin	7 (2.9)	2 (0.9)	9 (1.9)
Lyrica	2 (0.8)	0	2 (0.4)
Pregabaline	1 (0.4)	2 (0.9)	3 (0.6)
OTHER ANALGESICS AND ANTIPYRETICS	163 (68.2)	156 (67.2)	319 (67.7)
Paracetamol	99 (41.4)	90 (38.8)	189 (40.1)
Metamizol	41 (17.2)	60 (25.9)	101 (21.4)
Acetaminophen	23 (9.6)	20 (8.6)	43 (9.1)
Novaminsulfon	13 (5.4)	4 (1.7)	17 (3.6)
Gabapentin	5 (2.1)	7 (3.0)	12 (2.5)
Optalgin	4 (1.7)	5 (2.2)	9 (1.9)
Dipyrone	6 (2.5)	2 (0.9)	8 (1.7)
Paracetamolo	2 (0.8)	5 (2.2)	7 (1.5)
Perfalgan	2 (0.8)	5 (2.2)	7 (1.5)
Paracetamole	2 (0.8)	4 (1.7)	6 (1.3)
Amitriptyline	2 (0.8)	2 (0.9)	4 (0.8)
Panodil	3 (1.3)	1 (0.4)	4 (0.8)
Metamizole	1 (0.4)	2 (0.9)	3 (0.6)
Novalgin (Metamizol Natrium)	2 (0.8)	1 (0.4)	3 (0.6)
Tylenol	2 (0.8)	1 (0.4)	3 (0.6)
Dafalgan	2 (0.8)	0	2 (0.4)
Gabapentine	0	2 (0.9)	2 (0.4)
Novalgin	1 (0.4)	1 (0.4)	2 (0.4)
Supramol	2 (0.8)	0	2 (0.4)
V-Dalgin	0	2 (0.9)	2 (0.4)
Acamol	1 (0.4)	0	1 (0.2)
Acetaminophen/Butalbitol/Caffeine	0	1 (0.4)	1 (0.2)

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Acupan	1 (0.4)	0	1 (0.2)
Amitriptiline	1 (0.4)	0	1 (0.2)
Amitriptylin	1 (0.4)	0	1 (0.2)
Carbamezapine	1 (0.4)	0	1 (0.2)
Dipyron	1 (0.4)	0	1 (0.2)
Dipyrone (Optalgin)	1 (0.4)	0	1 (0.2)
Metamiozol	1 (0.4)	0	1 (0.2)
Metamizol Natrium	0	1 (0.4)	1 (0.2)
Mexalen	1 (0.4)	0	1 (0.2)
Nefopam 20mg/2ml, Perfusion	1 (0.4)	0	1 (0.2)
Novalgin / Metamizol	1 (0.4)	0	1 (0.2)
Novalgin Containing 1g Metamizole Sodium Monohydrate	1 (0.4)	0	1 (0.2)
Novalgin Metamizol-Natrium 1 H2o	1 (0.4)	0	1 (0.2)
Novalgin, Contains 500 Mg Metamizole Sodium Monohydrate	0	1 (0.4)	1 (0.2)
Novalminsulfon	1 (0.4)	0	1 (0.2)
Novaminosulfon	1 (0.4)	0	1 (0.2)
Novaminsulfat	0	1 (0.4)	1 (0.2)
Novaminsulfon/ Metamizol	1 (0.4)	0	1 (0.2)
Paracetam0l	0	1 (0.4)	1 (0.2)
Paracetamol (Perfalgan)	1 (0.4)	0	1 (0.2)
Paracetamol 1000 Mg	0	1 (0.4)	1 (0.2)
Paracetamol 1000mg, Tablet	1 (0.4)	0	1 (0.2)
Paracetamol 1000mg/100ml, Perfusion	1 (0.4)	0	1 (0.2)
Paracetamol Braun	1 (0.4)	0	1 (0.2)
Paracetamol, 1000mg	1 (0.4)	0	1 (0.2)
Paracetamol, 500 Mg, Gel	0	1 (0.4)	1 (0.2)
Paracetamole (Acamol)	0	1 (0.4)	1 (0.2)
Paracetamole (Perfalgan)	0	1 (0.4)	1 (0.2)
Paracetamolum	1 (0.4)	0	1 (0.2)
Paracetemol	0	1 (0.4)	1 (0.2)
Paracethamol	1 (0.4)	0	1 (0.2)
Pregabaline 25 Mg, Gel	0	1 (0.4)	1 (0.2)
Pregablin	1 (0.4)	0	1 (0.2)
Pyralgin / Metamizole	1 (0.4)	0	1 (0.2)
OTHER ANTIBACTERIALS	28 (11.7)	26 (11.2)	54 (11.5)
Vancomycin	7 (2.9)	8 (3.4)	15 (3.2)
Metronidazole	6 (2.5)	2 (0.9)	8 (1.7)
Metronidazol	3 (1.3)	2 (0.9)	5 (1.1)
Fosfomycin	3 (1.3)	1 (0.4)	4 (0.8)
Nitrofurantoine	2 (0.8)	2 (0.9)	4 (0.8)
Linezolid	2 (0.8)	1 (0.4)	3 (0.6)
Nitrofurantoin	1 (0.4)	2 (0.9)	3 (0.6)
Fosfomycine	0	2 (0.9)	2 (0.4)
Vancomycine	1 (0.4)	1 (0.4)	2 (0.4)
Fosfomicine	0	1 (0.4)	1 (0.2)
Furadantine	1 (0.4)	0	1 (0.2)
Lnezolid	1 (0.4)	0	1 (0.2)
Macrobid	0	1 (0.4)	1 (0.2)
Metronidazol (Flagyl)	0	1 (0.4)	1 (0.2)
Metronizadol	1 (0.4)	0	1 (0.2)
Nitrofurantoin Monohydrate	1 (0.4)	0	1 (0.2)
Nitrofurantoâ¯ne	1 (0.4)	0	1 (0.2)
Nitrufurantoine	0	1 (0.4)	1 (0.2)
Teicoplanin	1 (0.4)	0	1 (0.2)

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Vancomicine	0	1 (0.4)	1 (0.2)
Vancomycin Hydrochloride	1 (0.4)	0	1 (0.2)
Vancomycin Sodium Chloride	0	1 (0.4)	1 (0.2)
OTHER ANTIDIARRHEALS	1 (0.4)	1 (0.4)	2 (0.4)
Questran	1 (0.4)	0	1 (0.2)
Racecadotril	0	1 (0.4)	1 (0.2)
OTHER ANTIHYPERTENSIVES	0	1 (0.4)	1 (0.2)
Tadalafil	0	1 (0.4)	1 (0.2)
OTHER ANTINEOPLASTIC AGENTS	3 (1.3)	0	3 (0.6)
Hydrea	1 (0.4)	0	1 (0.2)
Hydroksikarbamid	1 (0.4)	0	1 (0.2)
Hydroxykarbamid	1 (0.4)	0	1 (0.2)
Litalir	1 (0.4)	0	1 (0.2)
OTHER BETA-LACTAM ANTIBACTERIALS	55 (23.0)	46 (19.8)	101 (21.4)
Ceftriaxone	11 (4.6)	13 (5.6)	24 (5.1)
Ceftriaxon	10 (4.2)	12 (5.2)	22 (4.7)
Meropenem	11 (4.6)	5 (2.2)	16 (3.4)
Cefazolin	4 (1.7)	6 (2.6)	10 (2.1)
Cefuroxim	5 (2.1)	3 (1.3)	8 (1.7)
Cefuroxime	5 (2.1)	1 (0.4)	6 (1.3)
Cefotaxim	2 (0.8)	3 (1.3)	5 (1.1)
Cefepime	2 (0.8)	0	2 (0.4)
Cefotaxime	1 (0.4)	1 (0.4)	2 (0.4)
Ceftazidim	2 (0.8)	0	2 (0.4)
Ceftazidime	1 (0.4)	1 (0.4)	2 (0.4)
Ceftriaxone Vit	0	2 (0.9)	2 (0.4)
Biotrakson/Ceftriaxon	1 (0.4)	0	1 (0.2)
Cefapime	1 (0.4)	0	1 (0.2)
Cefazolin "sandoz"	0	1 (0.4)	1 (0.2)
Cefazolin Sodium	0	1 (0.4)	1 (0.2)
Cefazoline	0	1 (0.4)	1 (0.2)
Cefriaxone	1 (0.4)	0	1 (0.2)
Ceftriaxone Ivpb 1g	0	1 (0.4)	1 (0.2)
Ceftriazone	0	1 (0.4)	1 (0.2)
Cefuroxine	1 (0.4)	0	1 (0.2)
Cephalexin	1 (0.4)	0	1 (0.2)
Meronem	1 (0.4)	0	1 (0.2)
Meroprenam	0	1 (0.4)	1 (0.2)
Merrem	1 (0.4)	0	1 (0.2)
Ospexin	1 (0.4)	0	1 (0.2)
Rocephin	0	1 (0.4)	1 (0.2)
Zinnat	1 (0.4)	0	1 (0.2)
OTHER CARDIAC PREPARATIONS	2 (0.8)	1 (0.4)	3 (0.6)
Coenzyme Q10	1 (0.4)	0	1 (0.2)
Trimetazidine	1 (0.4)	0	1 (0.2)
Trimethazidine	0	1 (0.4)	1 (0.2)
OTHER DERMATOLOGICAL PREPARATIONS	1 (0.4)	0	1 (0.2)
Dermitopic 0.1 %	1 (0.4)	0	1 (0.2)

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OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM	1 (0.4)	0	1 (0.2)
Quinine Sulfate	1 (0.4)	0	1 (0.2)
Beclometason	1 (0.4)	0	1 (0.2)
Fluticasone Propionate	1 (0.4)	1 (0.4)	2 (0.4)
Budesonide	1 (0.4)	5 (2.2)	6 (1.3)
Ipratropium Bromide	3 (1.3)	7 (3.0)	10 (2.1)
OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS	32 (13.4)	36 (15.5)	68 (14.4)
Atrovent	6 (2.5)	4 (1.7)	10 (2.1)
Ipratropiumbromid	5 (2.1)	2 (0.9)	7 (1.5)
Ipratropium	3 (1.3)	3 (1.3)	6 (1.3)
Fluticasone	2 (0.8)	1 (0.4)	3 (0.6)
Tiotropium	3 (1.3)	0	3 (0.6)
Fluticason	2 (0.8)	0	2 (0.4)
Glycopyrronium	2 (0.8)	0	2 (0.4)
Ipratromiumbromid	0	2 (0.9)	2 (0.4)
Mometasone	1 (0.4)	1 (0.4)	2 (0.4)
Pulmicort	1 (0.4)	1 (0.4)	2 (0.4)
Tiotropio	0	2 (0.9)	2 (0.4)
Alvesco Aerosol	0	1 (0.4)	1 (0.2)
Atroaldo	1 (0.4)	0	1 (0.2)
Beclohexal Da	0	1 (0.4)	1 (0.2)
Beclometasone Diproprionato	1 (0.4)	0	1 (0.2)
Beclomethason	1 (0.4)	0	1 (0.2)
Bromur Of Ipratropi	0	1 (0.4)	1 (0.2)
Budenosid	1 (0.4)	0	1 (0.2)
Budesonid	1 (0.4)	0	1 (0.2)
Inn-Glycopyrronium	0	1 (0.4)	1 (0.2)
Ipathropicum	0	1 (0.4)	1 (0.2)
Ipatropio	0	1 (0.4)	1 (0.2)
Ipatropio (Atrovent)	0	1 (0.4)	1 (0.2)
Ipatropium	0	1 (0.4)	1 (0.2)
Iprathropiumbromid	0	1 (0.4)	1 (0.2)
Ipratopio	0	1 (0.4)	1 (0.2)
Ipratopium	0	1 (0.4)	1 (0.2)
Ipratropio Bromuro	1 (0.4)	0	1 (0.2)
Ipratropium Bromid	0	1 (0.4)	1 (0.2)
Ipratropium Inhalation Liquid	1 (0.4)	0	1 (0.2)
Ipratropiumbromid 250âµg/2ml	1 (0.4)	0	1 (0.2)
Iptratromiumbromid	1 (0.4)	0	1 (0.2)
Pratropium Bromid	1 (0.4)	0	1 (0.2)
Spiriva	0	1 (0.4)	1 (0.2)
Spiriva Respimat	1 (0.4)	0	1 (0.2)
Tiotropium (Spiriva Respimat)	0	1 (0.4)	1 (0.2)
Umeclidinium	0	1 (0.4)	1 (0.2)
OTHER GYNECOLOGICALS	1 (0.4)	0	1 (0.2)
Dostinex	1 (0.4)	0	1 (0.2)
Natriumchlorid	0	1 (0.4)	1 (0.2)
Hidroxid Of Magnesium	0	1 (0.4)	1 (0.2)
Magnesium Oxide	1 (0.4)	0	1 (0.2)
Nacl	0	1 (0.4)	1 (0.2)
Sodium Chloride	1 (0.4)	3 (1.3)	4 (0.8)
Magnesium	7 (2.9)	9 (3.9)	16 (3.4)

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Nacl 0.9%	0	1 (0.4)	1 (0.2)
OTHER MINERAL SUPPLEMENTS	18 (7.5)	21 (9.1)	39 (8.3)
K-Phos Neutral Tab	0	1 (0.4)	1 (0.2)
Kochsalztabl.	0	1 (0.4)	1 (0.2)
Mag 2	1 (0.4)	0	1 (0.2)
Magenisum	0	1 (0.4)	1 (0.2)
Magnesi Lactici	1 (0.4)	0	1 (0.2)
Magnesium Gluconate	1 (0.4)	0	1 (0.2)
Magnesium Verla	1 (0.4)	0	1 (0.2)
Magnesiumaspartat	0	1 (0.4)	1 (0.2)
Magnesiumhydrogenaspartat	0	1 (0.4)	1 (0.2)
Magnesiumhydroxide	1 (0.4)	0	1 (0.2)
Magnosolv	1 (0.4)	0	1 (0.2)
Magnosolv Granulat	0	1 (0.4)	1 (0.2)
Monosodium Phosphate	0	1 (0.4)	1 (0.2)
Nacl 1g	1 (0.4)	0	1 (0.2)
Nacl Tablets	0	1 (0.4)	1 (0.2)
Phosphate Sandoz	0	1 (0.4)	1 (0.2)
Phosphoneuros	1 (0.4)	0	1 (0.2)
Phosphore Effervescent	1 (0.4)	0	1 (0.2)
Zinklet	1 (0.4)	0	1 (0.2)
OTHER NERVOUS SYSTEM DRUGS	0	2 (0.9)	2 (0.4)
Cerebrolysin	0	1 (0.4)	1 (0.2)
Propranolol	0	1 (0.4)	1 (0.2)
OTHER NUTRIENTS	12 (5.0)	12 (5.2)	24 (5.1)
Nutrison	3 (1.3)	2 (0.9)	5 (1.1)
Enteral Nutrition	1 (0.4)	2 (0.9)	3 (0.6)
Glucerna Plus	0	2 (0.9)	2 (0.4)
Osmolite	1 (0.4)	1 (0.4)	2 (0.4)
Enteral Nutrition (Promote)	0	1 (0.4)	1 (0.2)
Fish Oil	0	1 (0.4)	1 (0.2)
Fortimel Compact 2.4	1 (0.4)	0	1 (0.2)
Fresubin	1 (0.4)	0	1 (0.2)
Fresubin Energy Fibre	1 (0.4)	0	1 (0.2)
Isosource Protein Fibre	0	1 (0.4)	1 (0.2)
Jevity Plus	0	1 (0.4)	1 (0.2)
Jevity Rth	0	1 (0.4)	1 (0.2)
Nepro Hp	1 (0.4)	0	1 (0.2)
Novasource Gi Forte	1 (0.4)	0	1 (0.2)
Novasource Gi-Control	0	1 (0.4)	1 (0.2)
Nutrison Advanced Diason Optri	1 (0.4)	0	1 (0.2)
Nutrison Diabetes	0	1 (0.4)	1 (0.2)
Nutrison Protein Plus	1 (0.4)	0	1 (0.2)
Nutrison Proteä¯n Intense	1 (0.4)	0	1 (0.2)
Nutritional Formula (Glucerna Plus)	0	1 (0.4)	1 (0.2)
OTHER OPHTHALMOLOGICALS	12 (5.0)	5 (2.2)	17 (3.6)
Carbomeer Eyedrops	1 (0.4)	0	1 (0.2)
Corneregel	1 (0.4)	0	1 (0.2)
Dextran Hypromellose	0	1 (0.4)	1 (0.2)
Dextran/Hypromellose	1 (0.4)	0	1 (0.2)
Duratears	1 (0.4)	0	1 (0.2)
Duratears (Lanoline,paraffine, Vaseline)	1 (0.4)	0	1 (0.2)

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Hyabak	1 (0.4)	0	1 (0.2)
Hydroxyethylcellulose	0	1 (0.4)	1 (0.2)
Hylan Eyedrops	1 (0.4)	0	1 (0.2)
Hylo Gel	1 (0.4)	0	1 (0.2)
Hylo-Comod Drops	1 (0.4)	0	1 (0.2)
Hylocomod	1 (0.4)	0	1 (0.2)
Hypromellose	1 (0.4)	0	1 (0.2)
Normal Saline Eye Drops	0	1 (0.4)	1 (0.2)
Ocular Lubricant Bilaterally	1 (0.4)	0	1 (0.2)
Systane	0	1 (0.4)	1 (0.2)
Vismed	0	1 (0.4)	1 (0.2)
OTHER PLAIN VITAMIN PREPARATIONS	2 (0.8)	0	2 (0.4)
Pyridoxin	1 (0.4)	0	1 (0.2)
Pyridoxine	1 (0.4)	0	1 (0.2)
Diamox	1 (0.4)	0	1 (0.2)
OTHER RESPIRATORY SYSTEM PRODUCTS	1 (0.4)	0	1 (0.2)
OTHER VITAMIN PRODUCTS, COMBINATIONS	4 (1.7)	5 (2.2)	9 (1.9)
Multivitamin	2 (0.8)	2 (0.9)	4 (0.8)
Multivitamin With Minerals	1 (0.4)	1 (0.4)	2 (0.4)
Dagravit Multivitamin	0	1 (0.4)	1 (0.2)
Multi-Vitamin	1 (0.4)	0	1 (0.2)
Vitamin B	0	1 (0.4)	1 (0.2)
PARASYMPATHOMIMETICS	1 (0.4)	1 (0.4)	2 (0.4)
Neostigmin	1 (0.4)	0	1 (0.2)
Pyridostigmin	0	1 (0.4)	1 (0.2)
PERIPHERAL VASODILATORS	1 (0.4)	0	1 (0.2)
Polfilin / Pentoxifylline	1 (0.4)	0	1 (0.2)
POSTERIOR PITUITARY LOBE HORMONES	1 (0.4)	0	1 (0.2)
Desmopressin	1 (0.4)	0	1 (0.2)
Kalium	5 (2.1)	3 (1.3)	8 (1.7)
Potassium Chloride	14 (5.9)	10 (4.3)	24 (5.1)
Kaliumchlorid	3 (1.3)	2 (0.9)	5 (1.1)
Potassium Phosphate	0	1 (0.4)	1 (0.2)
Kcl	3 (1.3)	1 (0.4)	4 (0.8)
Kaliumchloride	1 (0.4)	4 (1.7)	5 (1.1)
Potassium	6 (2.5)	5 (2.2)	11 (2.3)
Potassium Chlorid	0	1 (0.4)	1 (0.2)
POTASSIUM	68 (28.5)	51 (22.0)	119 (25.3)
Kalinor	10 (4.2)	10 (4.3)	20 (4.2)
Kalium Verla	3 (1.3)	3 (1.3)	6 (1.3)
Kaliumcitrat	4 (1.7)	2 (0.9)	6 (1.3)
Diffu-K	2 (0.8)	0	2 (0.4)
Kalinor Retard	0	2 (0.9)	2 (0.4)
Kalioral (Trikaliumcitrat, Kaliumhydrogencarbonat, Citric Acid)	1 (0.4)	1 (0.4)	2 (0.4)
Kalnormin	2 (0.8)	0	2 (0.4)
Diffu K	0	1 (0.4)	1 (0.2)
Diffu K, 600 Mg	1 (0.4)	0	1 (0.2)
Diffuk	0	1 (0.4)	1 (0.2)

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K-10	1 (0.4)	0	1 (0.2)
K-Dur	1 (0.4)	0	1 (0.2)
K-Lyte	0	1 (0.4)	1 (0.2)
K/Mg-Aspartat	1 (0.4)	0	1 (0.2)
Kalinorâ® 1.56 G Potassium/2.5 G Citrate Effervescent Tablets	1 (0.4)	0	1 (0.2)
Kaliopoz	1 (0.4)	0	1 (0.2)
Kalioral	1 (0.4)	0	1 (0.2)
Kalioral "fresenius" - Pulver	0	1 (0.4)	1 (0.2)
Kalipoz	1 (0.4)	0	1 (0.2)
Kalipoz (Potassium Chloride)	0	1 (0.4)	1 (0.2)
Kalipoz / 391 Mg Potassium	1 (0.4)	0	1 (0.2)
Kalipoz Prolongatum	1 (0.4)	0	1 (0.2)
Kalium Chloratum	0	1 (0.4)	1 (0.2)
Kalium Citrate	1 (0.4)	0	1 (0.2)
Kalium Effervenscens	1 (0.4)	0	1 (0.2)
Kalium Effervescens	1 (0.4)	0	1 (0.2)
Kalium Effervescens (Potassium Chloride)	0	1 (0.4)	1 (0.2)
Kaliumcitrat Desmar	0	1 (0.4)	1 (0.2)
Kaliumcitrate	1 (0.4)	0	1 (0.2)
Kaliumhydrogentartrat	1 (0.4)	0	1 (0.2)
Kaliumklorid	1 (0.4)	0	1 (0.2)
Lentokalium	1 (0.4)	0	1 (0.2)
Micro K	1 (0.4)	0	1 (0.2)
Potassio Cloruro	0	1 (0.4)	1 (0.2)
Potassium Bicarb	0	1 (0.4)	1 (0.2)
Potassium Bicarbonate-Citric Acid	1 (0.4)	0	1 (0.2)
Potassium Chloride (Kci)	1 (0.4)	0	1 (0.2)
Potassium Chloride Ion	1 (0.4)	0	1 (0.2)
Potassium Citrate	0	1 (0.4)	1 (0.2)
Potassium Citrate + Potassium Hydrogen Carbonate	1 (0.4)	0	1 (0.2)
Potassium Gluconate	0	1 (0.4)	1 (0.2)
Potassium Gluconate, Sirup	1 (0.4)	0	1 (0.2)
Trikalium Citricii	1 (0.4)	0	1 (0.2)
Ultra K	1 (0.4)	0	1 (0.2)
PROGESTOGENS	1 (0.4)	0	1 (0.2)
Progestan	1 (0.4)	0	1 (0.2)
PROGESTOGENS AND ESTROGENS IN COMBINATION	1 (0.4)	0	1 (0.2)
Trophigil	1 (0.4)	0	1 (0.2)
Mcp	1 (0.4)	1 (0.4)	2 (0.4)
Primperan	1 (0.4)	0	1 (0.2)
PROPULSIVES	8 (3.3)	5 (2.2)	13 (2.8)
Domperidone	1 (0.4)	1 (0.4)	2 (0.4)
Litican	1 (0.4)	0	1 (0.2)
Mcp Hexal	1 (0.4)	0	1 (0.2)
Metocloperamide	0	1 (0.4)	1 (0.2)
Metroclopamide	1 (0.4)	0	1 (0.2)
Metroclopramide	0	1 (0.4)	1 (0.2)
Motilium	1 (0.4)	0	1 (0.2)
Paspertin	1 (0.4)	0	1 (0.2)
Pramin	0	1 (0.4)	1 (0.2)
PROTEIN KINASE INHIBITORS	2 (0.8)	0	2 (0.4)

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ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Ruxolitinib	2 (0.8)	0	2 (0.4)
PROTEIN SUPPLEMENTS	3 (1.3)	2 (0.9)	5 (1.1)
Beneprotein	1 (0.4)	2 (0.9)	3 (0.6)
Easy Whey	1 (0.4)	0	1 (0.2)
Protein	1 (0.4)	0	1 (0.2)
PSYCHOSTIMULANTS, AGENTS USED FOR ADHD AND NOOTROPICS	3 (1.3)	0	3 (0.6)
Modafinil	2 (0.8)	0	2 (0.4)
Methylphenidate	1 (0.4)	0	1 (0.2)
Modinafil	1 (0.4)	0	1 (0.2)
Ofloxacine	0	1 (0.4)	1 (0.2)
QUINOLONE ANTIBACTERIALS	15 (6.3)	14 (6.0)	29 (6.2)
Ciprofloxacin	6 (2.5)	4 (1.7)	10 (2.1)
Ciprofloxacine	3 (1.3)	2 (0.9)	5 (1.1)
Levofloxacin	2 (0.8)	3 (1.3)	5 (1.1)
Ciproxin	1 (0.4)	1 (0.4)	2 (0.4)
Levofloxacine	2 (0.8)	0	2 (0.4)
Ciprobay	0	1 (0.4)	1 (0.2)
Ciprofloxacillin	1 (0.4)	0	1 (0.2)
Ciprofloxacina	0	1 (0.4)	1 (0.2)
Citrofloxacin	1 (0.4)	0	1 (0.2)
Tavanic	0	1 (0.4)	1 (0.2)
Diltiazem	1 (0.4)	2 (0.9)	3 (0.6)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CARDIAC EFFECTS	9 (3.8)	8 (3.4)	17 (3.6)
Verapamil	4 (1.7)	5 (2.2)	9 (1.9)
Diltiazem Hcl	0	1 (0.4)	1 (0.2)
Dilzene	1 (0.4)	0	1 (0.2)
Monotildiem Lp	1 (0.4)	0	1 (0.2)
Verapamil Hydrochlorid	1 (0.4)	0	1 (0.2)
Verapress	1 (0.4)	0	1 (0.2)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	166 (69.5)	154 (66.4)	320 (67.9)
Amlodipin	56 (23.4)	55 (23.7)	111 (23.6)
Amlodipine	50 (20.9)	48 (20.7)	98 (20.8)
Nicardipine	17 (7.1)	27 (11.6)	44 (9.3)
Nifedipin	11 (4.6)	5 (2.2)	16 (3.4)
Lercanidipin	8 (3.3)	5 (2.2)	13 (2.8)
Nitrendipin	6 (2.5)	6 (2.6)	12 (2.5)
Nifedipine	6 (2.5)	5 (2.2)	11 (2.3)
Lercanidipine	6 (2.5)	4 (1.7)	10 (2.1)
Amlodipina	2 (0.8)	5 (2.2)	7 (1.5)
Loxen	5 (2.1)	2 (0.9)	7 (1.5)
Nimodipin	3 (1.3)	2 (0.9)	5 (1.1)
Vasodip	4 (1.7)	1 (0.4)	5 (1.1)
Amlodibene	3 (1.3)	1 (0.4)	4 (0.8)
Amlor	2 (0.8)	2 (0.9)	4 (0.8)
Amlow	2 (0.8)	2 (0.9)	4 (0.8)
Clevidipine	1 (0.4)	3 (1.3)	4 (0.8)
Norvasc	3 (1.3)	0	3 (0.6)
Rydene	2 (0.8)	1 (0.4)	3 (0.6)
Zanidip	3 (1.3)	0	3 (0.6)
Agen	2 (0.8)	0	2 (0.4)

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ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Amlodipino	0	2 (0.9)	2 (0.4)
Amlopidine	0	2 (0.9)	2 (0.4)
Amplodipine	1 (0.4)	1 (0.4)	2 (0.4)
Cleviprex	0	2 (0.9)	2 (0.4)
Lecardipine	0	2 (0.9)	2 (0.4)
Nircadipine	1 (0.4)	1 (0.4)	2 (0.4)
Adalat	1 (0.4)	0	1 (0.2)
Almodipin	0	1 (0.4)	1 (0.2)
Amlodipin Besilat	1 (0.4)	0	1 (0.2)
Amlodipine 5mg, Caps	0	1 (0.4)	1 (0.2)
Amlodipine Maleate (Amlow)	0	1 (0.4)	1 (0.2)
Amlodipn	1 (0.4)	0	1 (0.2)
Amlodistad	1 (0.4)	0	1 (0.2)
Amlodopine	1 (0.4)	0	1 (0.2)
Amlopdipine	0	1 (0.4)	1 (0.2)
Amlopin (Amlodipine)	0	1 (0.4)	1 (0.2)
Amlopin (Amlodypine)	0	1 (0.4)	1 (0.2)
Amodipine	0	1 (0.4)	1 (0.2)
Amplidipine	1 (0.4)	0	1 (0.2)
Ampodipin	1 (0.4)	0	1 (0.2)
Barnidipine	0	1 (0.4)	1 (0.2)
Cardene	0	1 (0.4)	1 (0.2)
Cleviprex Ijem	1 (0.4)	0	1 (0.2)
Clonidipin	0	1 (0.4)	1 (0.2)
Felodipin	0	1 (0.4)	1 (0.2)
Isradipine	1 (0.4)	0	1 (0.2)
Lecaranidipine	0	1 (0.4)	1 (0.2)
Lecarnidipin	0	1 (0.4)	1 (0.2)
Lercadipine 10mg	1 (0.4)	0	1 (0.2)
Lercandipini	1 (0.4)	0	1 (0.2)
Lercanidipine 10mg, Tablet	1 (0.4)	0	1 (0.2)
Lercanipidine	1 (0.4)	0	1 (0.2)
Lercarnidipin	1 (0.4)	0	1 (0.2)
Nicardipine 20 Mg/20ml	1 (0.4)	0	1 (0.2)
Nicardipine 20 Mg/20ml, Perfusion	0	1 (0.4)	1 (0.2)
Nicardipine 20mg, Cp	0	1 (0.4)	1 (0.2)
Nicardipine 75mg/150ml 0.9% Nacl Solution	1 (0.4)	0	1 (0.2)
Nicardipine Chlorydrate	0	1 (0.4)	1 (0.2)
Nicardipine Hydrochloride	1 (0.4)	0	1 (0.2)
Nicardipine In Sodium Chloride 40 Mg-0.83/200 Ml Premix Iv Infusion	0	1 (0.4)	1 (0.2)
Nicardipine Inet	1 (0.4)	0	1 (0.2)
Nicardipine/Sodium Chloride	0	1 (0.4)	1 (0.2)
Nicarpidine	0	1 (0.4)	1 (0.2)
Nifedepine	0	1 (0.4)	1 (0.2)
Nifedipine Retard	1 (0.4)	0	1 (0.2)
Nifedipine Retard Eg	1 (0.4)	0	1 (0.2)
Nifendipin	0	1 (0.4)	1 (0.2)
Nifidepin	1 (0.4)	0	1 (0.2)
Nimodipine	0	1 (0.4)	1 (0.2)
Nimotop	1 (0.4)	0	1 (0.2)
Nircadipine 20mg, Tablet	1 (0.4)	0	1 (0.2)
Nircadipine 20mg/20ml, Perfusion	1 (0.4)	0	1 (0.2)
Norvasc (Amlodipina)	0	1 (0.4)	1 (0.2)
Norvask	1 (0.4)	0	1 (0.2)
Primacor / Lercanidipine	1 (0.4)	0	1 (0.2)

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Chlorhexidine	0	1 (0.4)	1 (0.2)
Nystatin	0	4 (1.7)	4 (0.8)
STOMATOLOGICAL PREPARATIONS	5 (2.1)	8 (3.4)	13 (2.8)
Artificial Saliva Gel	1 (0.4)	0	1 (0.2)
Biotene Oral Mouth Rinse	1 (0.4)	0	1 (0.2)
Bioxtra Dry Mouth Oral Gel	1 (0.4)	0	1 (0.2)
Chlorihexidine	0	1 (0.4)	1 (0.2)
Dentio Spray	1 (0.4)	0	1 (0.2)
Glandomed	1 (0.4)	0	1 (0.2)
Jack Pro	1 (0.4)	0	1 (0.2)
Miconazol Oral Gel	0	1 (0.4)	1 (0.2)
Miconazole 2%, Daktarin	0	1 (0.4)	1 (0.2)
Moisturizing Mouth Spray	0	1 (0.4)	1 (0.2)
Procor	1 (0.4)	2 (0.9)	3 (0.6)
SULFONAMIDES AND TRIMETHOPRIM	9 (3.8)	10 (4.3)	19 (4.0)
Cotrimoxazol	1 (0.4)	2 (0.9)	3 (0.6)
Bactrim Ds	0	1 (0.4)	1 (0.2)
Co-Trimoxazol	1 (0.4)	0	1 (0.2)
Cotimoxazol	1 (0.4)	0	1 (0.2)
Cotrim	0	1 (0.4)	1 (0.2)
Cotrimossazolo	0	1 (0.4)	1 (0.2)
Cotrimoxazole	0	1 (0.4)	1 (0.2)
Eusaprim	1 (0.4)	0	1 (0.2)
Sulfamethoxazole (Bactrim Ds)	1 (0.4)	0	1 (0.2)
Sulfamethoxazole/Trimethoprim 160/800 Mg	1 (0.4)	0	1 (0.2)
Sulfamethoxazoletrimethoprim	0	1 (0.4)	1 (0.2)
Trimethoprim, Sulphamethoxazole	1 (0.4)	0	1 (0.2)
Trimethoprim-Sulfamethoxazole	0	1 (0.4)	1 (0.2)
Trimethoprime (Bactrim Ds)	1 (0.4)	0	1 (0.2)
Trimetoprime	1 (0.4)	0	1 (0.2)
SURGICAL AIDS	2 (0.8)	0	2 (0.4)
Hyaluron Eyedrops	1 (0.4)	0	1 (0.2)
Hydroxypropylmethylcellulose	1 (0.4)	0	1 (0.2)
TETRACYCLINES	1 (0.4)	0	1 (0.2)
Doxycycline	1 (0.4)	0	1 (0.2)
THYROID PREPARATIONS	43 (18.0)	41 (17.7)	84 (17.8)
L-Thyroxin	9 (3.8)	6 (2.6)	15 (3.2)
Levothyroxin	9 (3.8)	6 (2.6)	15 (3.2)
Levothyroxine	6 (2.5)	9 (3.9)	15 (3.2)
Euthyrox	6 (2.5)	1 (0.4)	7 (1.5)
Levothyrox	2 (0.8)	3 (1.3)	5 (1.1)
L-Thyroxine	2 (0.8)	2 (0.9)	4 (0.8)
Levotiroxina	0	4 (1.7)	4 (0.8)
Synthroid	1 (0.4)	2 (0.9)	3 (0.6)
Eltroxin	1 (0.4)	1 (0.4)	2 (0.4)
L-Thyrox	2 (0.8)	0	2 (0.4)
Levothyroxine Sodium	0	2 (0.9)	2 (0.4)
Eutirox	1 (0.4)	0	1 (0.2)
L Thyroxin	1 (0.4)	0	1 (0.2)
L Tyroxin	1 (0.4)	0	1 (0.2)

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L- Thyroxin	0	1 (0.4)	1 (0.2)
L-Thyroxin Henning	1 (0.4)	0	1 (0.2)
L-Tyhroxin	1 (0.4)	0	1 (0.2)
Levathyroxin	0	1 (0.4)	1 (0.2)
Levothroxin	0	1 (0.4)	1 (0.2)
Levotiroxine	0	1 (0.4)	1 (0.2)
Lã©vothyroxine	0	1 (0.4)	1 (0.2)
T4	1 (0.4)	0	1 (0.2)
Thyrax	0	1 (0.4)	1 (0.2)
Diclofenac	1 (0.4)	3 (1.3)	4 (0.8)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	5 (2.1)	8 (3.4)	13 (2.8)
Diclofenac Diethylamine	1 (0.4)	1 (0.4)	2 (0.4)
Voltaren Emulgel	1 (0.4)	1 (0.4)	2 (0.4)
Deep Relief Menthol 2 %	1 (0.4)	0	1 (0.2)
Diclofenac Diethylamin	0	1 (0.4)	1 (0.2)
Diclofenac Epolamine	0	1 (0.4)	1 (0.2)
Diclofenac Gel	1 (0.4)	0	1 (0.2)
Voltaren	0	1 (0.4)	1 (0.2)
ULTRASOUND CONTRAST MEDIA	1 (0.4)	0	1 (0.2)
Perflutren Lipid Microspheres	1 (0.4)	0	1 (0.2)
Methionin	2 (0.8)	1 (0.4)	3 (0.6)
UROLOGICALS	22 (9.2)	7 (3.0)	29 (6.2)
Solifenacin	4 (1.7)	1 (0.4)	5 (1.1)
Mirabegron	3 (1.3)	0	3 (0.6)
Betmiga	1 (0.4)	1 (0.4)	2 (0.4)
Solifenacine	1 (0.4)	1 (0.4)	2 (0.4)
Fesoterodine (Toviaz) Lp 8 Mg	1 (0.4)	0	1 (0.2)
Inkontan	1 (0.4)	0	1 (0.2)
Oxybutinin	1 (0.4)	0	1 (0.2)
Oxybutynin	1 (0.4)	0	1 (0.2)
Oxybutynine	0	1 (0.4)	1 (0.2)
Phenazopyridine	1 (0.4)	0	1 (0.2)
Phenazopyridine Hydrochloride	1 (0.4)	0	1 (0.2)
Potassium Citrate, Mixture 33 Mg K+/Ml:	0	1 (0.4)	1 (0.2)
Propiverinhydrochlorid	1 (0.4)	0	1 (0.2)
Solfenacinesuccinaat	1 (0.4)	0	1 (0.2)
Solifinacinsuccinat	1 (0.4)	0	1 (0.2)
Spasmex	1 (0.4)	0	1 (0.2)
Tolterodin	1 (0.4)	0	1 (0.2)
Tolterodin Acc	1 (0.4)	0	1 (0.2)
Trospium	0	1 (0.4)	1 (0.2)
Trospiumchlorid	1 (0.4)	0	1 (0.2)
VASODILATORS USED IN CARDIAC DISEASES	24 (10.0)	20 (8.6)	44 (9.3)
Nitroglycerin	0	4 (1.7)	4 (0.8)
Glyceryl Trinitrate	2 (0.8)	1 (0.4)	3 (0.6)
Nitroglycerine	3 (1.3)	0	3 (0.6)
Nitrolingual	2 (0.8)	1 (0.4)	3 (0.6)
Nitrolingual Spray	1 (0.4)	2 (0.9)	3 (0.6)
Coruno Retard	1 (0.4)	1 (0.4)	2 (0.4)
Epinitril	0	2 (0.9)	2 (0.4)
Minitran	1 (0.4)	1 (0.4)	2 (0.4)

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Nitro Spray	0	2 (0.9)	2 (0.4)
Nitroglicerina	1 (0.4)	1 (0.4)	2 (0.4)
Sacubitril	1 (0.4)	1 (0.4)	2 (0.4)
Cedocard	1 (0.4)	0	1 (0.2)
Glyceril Trinitras	1 (0.4)	0	1 (0.2)
Glycerin-Trinitrate	0	1 (0.4)	1 (0.2)
Glycerolnitrat	1 (0.4)	0	1 (0.2)
Glyceryl Trinitrate 50mg/50ml Infusion	0	1 (0.4)	1 (0.2)
Glyceryli Trinitras	1 (0.4)	0	1 (0.2)
Glyceryltrinitrat	1 (0.4)	0	1 (0.2)
Imdur	1 (0.4)	0	1 (0.2)
Isosorbide Dinitrate	1 (0.4)	0	1 (0.2)
Isosorbide Mononitrate	0	1 (0.4)	1 (0.2)
Isosorbidedinitraat	0	1 (0.4)	1 (0.2)
Isosorbidemononitraat	0	1 (0.4)	1 (0.2)
Isosorbitr Dinitrate	1 (0.4)	0	1 (0.2)
Melsidomin	1 (0.4)	0	1 (0.2)
Minitran Depot	1 (0.4)	0	1 (0.2)
Minitran Depotplaster	1 (0.4)	0	1 (0.2)
Molsidomin	1 (0.4)	0	1 (0.2)
Nitroglycerin Spray	1 (0.4)	0	1 (0.2)
Nitroglycerine Plaster	0	1 (0.4)	1 (0.2)
Nitrolingualspray	0	1 (0.4)	1 (0.2)
Pentalong	1 (0.4)	0	1 (0.2)
Trinitrine	0	1 (0.4)	1 (0.2)
VIRAL VACCINES	0	1 (0.4)	1 (0.2)
Influenza Vaccine High Dose	0	1 (0.4)	1 (0.2)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO	38 (15.9)	33 (14.2)	71 (15.1)
Colecalciferol	11 (4.6)	10 (4.3)	21 (4.5)
Cholecalciferol	4 (1.7)	5 (2.2)	9 (1.9)
Dekristol	1 (0.4)	6 (2.6)	7 (1.5)
Vitamin D	4 (1.7)	3 (1.3)	7 (1.5)
Vitamin D3	3 (1.3)	1 (0.4)	4 (0.8)
Zymad	1 (0.4)	2 (0.9)	3 (0.6)
D-Cure	1 (0.4)	1 (0.4)	2 (0.4)
Uvedose	2 (0.8)	0	2 (0.4)
Vigantoletten	1 (0.4)	1 (0.4)	2 (0.4)
Alfa D	1 (0.4)	0	1 (0.2)
Calcifediol	0	1 (0.4)	1 (0.2)
Calcitriol	1 (0.4)	0	1 (0.2)
Cholecalciferol Vitamin D	1 (0.4)	0	1 (0.2)
Colecalciferol (Vitamine D3)	1 (0.4)	0	1 (0.2)
Colecaliferol	1 (0.4)	0	1 (0.2)
Colicalciferol	1 (0.4)	0	1 (0.2)
D-Vitamin	1 (0.4)	0	1 (0.2)
Divisun	1 (0.4)	0	1 (0.2)
Etalpha	1 (0.4)	0	1 (0.2)
Hidroferol	0	1 (0.4)	1 (0.2)
Oleovit	0	1 (0.4)	1 (0.2)
Vitamin D2	0	1 (0.4)	1 (0.2)
Vitamine D	0	1 (0.4)	1 (0.2)
Vitamine D/ Colecalciferol	1 (0.4)	0	1 (0.2)
Zymad Vit D	1 (0.4)	0	1 (0.2)

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AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.3
Concomitant Medication
Safety Analysis Set

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
VITAMIN B-COMPLEX, INCL. COMBINATIONS	4 (1.7)	1 (0.4)	5 (1.1)
Apovit B-Combin Strong	1 (0.4)	0	1 (0.2)
Becozyme	0	1 (0.4)	1 (0.2)
Pabrinex	1 (0.4)	0	1 (0.2)
Vitamin B Combination: Cyanocobalamin (Vitamin B12), Folsyre, Pyridoxin (Vitamin B6)	1 (0.4)	0	1 (0.2)
Vitamine B Complex	1 (0.4)	0	1 (0.2)
VITAMIN B1, PLAIN AND IN COMBINATION WITH VITAMIN B6 AND B12	13 (5.4)	11 (4.7)	24 (5.1)
Thiamin	5 (2.1)	3 (1.3)	8 (1.7)
Thiamine	3 (1.3)	2 (0.9)	5 (1.1)
Vitamin B1	1 (0.4)	4 (1.7)	5 (1.1)
Befact Forte	1 (0.4)	0	1 (0.2)
Benerva	0	1 (0.4)	1 (0.2)
Thiamin Pyridoxin Cyanocobalamin	1 (0.4)	0	1 (0.2)
Vitamin Bâ,□	1 (0.4)	0	1 (0.2)
Vitamine B1 Ratio	1 (0.4)	0	1 (0.2)
Vitamine B6 + Bevitine	0	1 (0.4)	1 (0.2)
VITAMIN B12 AND FOLIC ACID	17 (7.1)	17 (7.3)	34 (7.2)
Folic Acid	9 (3.8)	8 (3.4)	17 (3.6)
Cyanocobalamin	4 (1.7)	1 (0.4)	5 (1.1)
Vitamin B12	2 (0.8)	3 (1.3)	5 (1.1)
Folsan	1 (0.4)	1 (0.4)	2 (0.4)
Acfol	0	1 (0.4)	1 (0.2)
Acide Folique	1 (0.4)	0	1 (0.2)
Betolvex	1 (0.4)	0	1 (0.2)
Betolvidon	0	1 (0.4)	1 (0.2)
Cyancocobalamin	0	1 (0.4)	1 (0.2)
Cyanokobalamine	0	1 (0.4)	1 (0.2)
Folic Acid 5 Mg, Cp	0	1 (0.4)	1 (0.2)
Folimet	1 (0.4)	0	1 (0.2)
Folsã¤ure	0	1 (0.4)	1 (0.2)
Hydroxocobalamine	1 (0.4)	0	1 (0.2)
Vitamin B-12	1 (0.4)	0	1 (0.2)
Vitamin B12 (Cyanocobalamin)	1 (0.4)	0	1 (0.2)
Vitamine B12	1 (0.4)	0	1 (0.2)
VITAMIN K AND OTHER HEMOSTATICS	12 (5.0)	19 (8.2)	31 (6.6)
Beriplex	0	5 (2.2)	5 (1.1)
Phytomenadion	4 (1.7)	1 (0.4)	5 (1.1)
Octaplex	1 (0.4)	2 (0.9)	3 (0.6)
Ppsb	2 (0.8)	1 (0.4)	3 (0.6)
Prothrombin Complex Concentrate	0	3 (1.3)	3 (0.6)
Vitamin K	1 (0.4)	2 (0.9)	3 (0.6)
Konakion	2 (0.8)	0	2 (0.4)
Phytonadione	1 (0.4)	1 (0.4)	2 (0.4)
Prothrombin Complex	2 (0.8)	0	2 (0.4)
Beriplex (Pcc)	0	1 (0.4)	1 (0.2)
Cofact	0	1 (0.4)	1 (0.2)
Factor 13	1 (0.4)	0	1 (0.2)
Faktor 8	1 (0.4)	0	1 (0.2)
Fibrinogen	0	1 (0.4)	1 (0.2)
Human Prothrombine Complex	0	1 (0.4)	1 (0.2)
Prothrombin Complex Concentrate (Pcc)	1 (0.4)	0	1 (0.2)

Concomitant medications are defined as medications that are started on or after the start of study treatment, or are ongoing at the start of study treatment.
For participants who are randomized into the usual care arm and receive no treatment, their randomization date is used as the start of study treatment.
Medications with partial dates are considered as both prior and concomitant if either type cannot be determined with certainty.
Concomitant medications are coded using WHODrug version Sep2022.
Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

Table 1.3
Concomitant Medication
Safety Analysis Set

ATC 3 Classification Generic Name	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)	Total (N=471) n (%)
Prothrombin Concentrate	1 (0.4)	0	1 (0.2)
Prothromplex	0	1 (0.4)	1 (0.2)
Surgiflo	1 (0.4)	0	1 (0.2)
Tachosil	1 (0.4)	0	1 (0.2)
Vit. K1	1 (0.4)	0	1 (0.2)
Vitamine K	1 (0.4)	0	1 (0.2)
X-RAY CONTRAST MEDIA, IODINATED	4 (1.7)	2 (0.9)	6 (1.3)
Iohexol	3 (1.3)	2 (0.9)	5 (1.1)
Gastrografin / Amidotrizoesã¤ure	1 (0.4)	0	1 (0.2)
X-RAY CONTRAST MEDIA, NON-IODINATED	1 (0.4)	1 (0.4)	2 (0.4)
Barium Sulfate	1 (0.4)	1 (0.4)	2 (0.4)
-- NOT CODED --	8 (3.3)	6 (2.6)	14 (3.0)
-- Not Coded --	3 (1.3)	0	3 (0.6)
Ensure	2 (0.8)	0	2 (0.4)
Passedan	1 (0.4)	1 (0.4)	2 (0.4)
Antibiotic (Name Unknown)	0	1 (0.4)	1 (0.2)
Food Complement	0	1 (0.4)	1 (0.2)
Nutrison Diason	1 (0.4)	0	1 (0.2)
Steroid Injection	0	1 (0.4)	1 (0.2)
Tc-99m Maa	1 (0.4)	0	1 (0.2)
Tc-99m Techengas	1 (0.4)	0	1 (0.2)
Thyronajod	0	1 (0.4)	1 (0.2)
Triad Cream	0	1 (0.4)	1 (0.2)

Concomitant medications are defined as medications that are started on or after the start of study treatment, or are ongoing at the start of study treatment.
For participants who are randomized into the usual care arm and receive no treatment, their randomization date is used as the start of study treatment.
Medications with partial dates are considered as both prior and concomitant if either type cannot be determined with certainty.
Concomitant medications are coded using WHODrug version Sep2022.
Sorting order: Alphabetical ATC class and then by descending frequency based on Total group.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.3.1
Concomitant Medication as Rescue Therapy
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)	Total (N=474)
	n (%)	n (%)	n (%)
Any Concomitant Medication	1 (0.4)	8 (3.4)	9 (1.9)

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.4.1
Medical History
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Overall	239	232
Blood and lymphatic system disorders	20 (8.4)	22 (9.5)
Anaemia	10 (4.2)	12 (5.2)
Autoimmune haemolytic anaemia	0	1 (0.4)
Febrile neutropenia	1 (0.4)	0
Granulomatous lymphadenitis	0	1 (0.4)
Heparin-induced thrombocytopenia	0	1 (0.4)
Hypochromic anaemia	1 (0.4)	0
Iron deficiency anaemia	1 (0.4)	1 (0.4)
Leukocytosis	1 (0.4)	0
Lymphadenopathy mediastinal	1 (0.4)	1 (0.4)
Microcytic anaemia	1 (0.4)	0
Normochromic normocytic anaemia	1 (0.4)	0
Pancytopenia	0	1 (0.4)
Polycythaemia	0	1 (0.4)
Splenomegaly	0	2 (0.9)
Thrombocytopenia	3 (1.3)	4 (1.7)
Thrombocytosis	1 (0.4)	0
Cardiac disorders	224 (93.7)	215 (92.7)
Acute coronary syndrome	13 (5.4)	7 (3.0)
Acute myocardial infarction	1 (0.4)	0
Angina pectoris	15 (6.3)	14 (6.0)
Angina unstable	3 (1.3)	3 (1.3)
Aortic valve incompetence	4 (1.7)	6 (2.6)
Aortic valve sclerosis	1 (0.4)	0
Aortic valve stenosis	2 (0.8)	1 (0.4)
Arrhythmia	0	1 (0.4)
Arteriosclerosis coronary artery	3 (1.3)	5 (2.2)
Atrial fibrillation	213 (89.1)	194 (83.6)
Atrial flutter	0	3 (1.3)
Atrioventricular block complete	3 (1.3)	0
Atrioventricular block first degree	3 (1.3)	3 (1.3)
Atrioventricular block second degree	1 (0.4)	1 (0.4)
Bradyarrhythmia	0	1 (0.4)
Bradycardia	3 (1.3)	5 (2.2)
Bundle branch block left	1 (0.4)	5 (2.2)
Bundle branch block right	1 (0.4)	4 (1.7)
Cardiac asthma	0	1 (0.4)
Cardiac failure	0	4 (1.7)
Cardiac failure chronic	2 (0.8)	0
Cardiac failure congestive	35 (14.6)	48 (20.7)
Cardiac valve disease	0	1 (0.4)
Cardiomyopathy	1 (0.4)	2 (0.9)
Cardiovascular insufficiency	1 (0.4)	0
Coronary artery disease	11 (4.6)	20 (8.6)
Coronary artery insufficiency	1 (0.4)	0
Coronary artery occlusion	1 (0.4)	0
Coronary artery stenosis	1 (0.4)	0
Diastolic dysfunction	0	2 (0.9)
Hypertensive cardiomyopathy	1 (0.4)	1 (0.4)
Hypertensive heart disease	1 (0.4)	0
Ischaemic cardiomyopathy	0	1 (0.4)
Left atrial dilatation	0	1 (0.4)
Left ventricular hypertrophy	0	1 (0.4)
Mitral valve incompetence	6 (2.5)	4 (1.7)
Myocardial infarction	26 (10.9)	31 (13.4)
Myocardial ischaemia	7 (2.9)	8 (3.4)
Palpitations	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Pericardial cyst	1 (0.4)	0
Pericardial effusion	0	1 (0.4)
Pericarditis	3 (1.3)	1 (0.4)
Sinus arrest	1 (0.4)	0
Sinus bradycardia	1 (0.4)	2 (0.9)
Sinus node dysfunction	4 (1.7)	3 (1.3)
Sinus tachycardia	0	2 (0.9)
Supraventricular tachycardia	4 (1.7)	3 (1.3)
Tachyarrhythmia	0	1 (0.4)
Tachycardia	0	1 (0.4)
Tricuspid valve incompetence	1 (0.4)	6 (2.6)
Trifascicular block	1 (0.4)	0
Ventricular extrasystoles	1 (0.4)	0
Ventricular tachycardia	1 (0.4)	0
Congenital, familial and genetic disorders	3 (1.3)	9 (3.9)
Atrial septal defect	0	3 (1.3)
Dermoid cyst	0	1 (0.4)
Factor VII deficiency	0	1 (0.4)
Gilbert's syndrome	0	2 (0.9)
Heart disease congenital	1 (0.4)	0
Hypoplastic left heart syndrome	0	1 (0.4)
Muscular dystrophy	1 (0.4)	0
Syndactyly	1 (0.4)	1 (0.4)
Ear and labyrinth disorders	8 (3.3)	3 (1.3)
Ear haemorrhage	0	1 (0.4)
Hypoacusis	1 (0.4)	0
Meniere's disease	0	2 (0.9)
Presbyacusis	1 (0.4)	0
Vertigo	4 (1.7)	1 (0.4)
Vertigo positional	2 (0.8)	0
Endocrine disorders	53 (22.2)	56 (24.1)
Adrenal insufficiency	0	2 (0.9)
Autoimmune thyroiditis	0	1 (0.4)
Goitre	6 (2.5)	2 (0.9)
Hyperparathyroidism	1 (0.4)	0
Hyperparathyroidism secondary	0	1 (0.4)
Hyperthyroidism	8 (3.3)	8 (3.4)
Hypoparathyroidism	1 (0.4)	0
Hypothyroidism	36 (15.1)	41 (17.7)
Thyroid disorder	0	1 (0.4)
Thyroid mass	2 (0.8)	0
Eye disorders	29 (12.1)	19 (8.2)
Age-related macular degeneration	1 (0.4)	0
Amaurosis fugax	0	1 (0.4)
Blindness	2 (0.8)	0
Blindness unilateral	0	2 (0.9)
Cataract	6 (2.5)	4 (1.7)
Diabetic retinopathy	1 (0.4)	2 (0.9)
Dry age-related macular degeneration	0	1 (0.4)
Epiretinal membrane	1 (0.4)	0
Eye disorder	0	1 (0.4)
Glaucoma	12 (5.0)	6 (2.6)
Macular degeneration	2 (0.8)	0
Neovascular age-related macular degeneration	1 (0.4)	0
Ocular hypertension	1 (0.4)	1 (0.4)
Optic ischaemic neuropathy	0	1 (0.4)
Retinal detachment	1 (0.4)	1 (0.4)

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Retinal haemorrhage	1 (0.4)	0
Retinopathy	1 (0.4)	0
Retinopathy hypertensive	1 (0.4)	0
Vitreous haemorrhage	1 (0.4)	0
Gastrointestinal disorders	65 (27.2)	53 (22.8)
Abdominal distension	0	1 (0.4)
Abdominal pain lower	0	1 (0.4)
Ascites	1 (0.4)	0
Barrett's oesophagus	2 (0.8)	1 (0.4)
Chronic gastritis	2 (0.8)	0
Coeliac disease	1 (0.4)	1 (0.4)
Colitis ischaemic	0	1 (0.4)
Colitis ulcerative	2 (0.8)	1 (0.4)
Constipation	10 (4.2)	7 (3.0)
Crohn's disease	4 (1.7)	0
Dental caries	0	1 (0.4)
Diaphragmatic hernia	1 (0.4)	0
Diverticulum	6 (2.5)	1 (0.4)
Diverticulum intestinal	3 (1.3)	2 (0.9)
Diverticulum intestinal haemorrhagic	0	1 (0.4)
Duodenal ulcer	0	1 (0.4)
Dyspepsia	5 (2.1)	0
Dysphagia	1 (0.4)	0
Gastric haemorrhage	0	1 (0.4)
Gastric ulcer	1 (0.4)	3 (1.3)
Gastritis	3 (1.3)	7 (3.0)
Gastritis alcoholic	1 (0.4)	0
Gastrointestinal angiodysplasia	0	1 (0.4)
Gastrointestinal haemorrhage	1 (0.4)	0
Gastrointestinal ulcer	1 (0.4)	1 (0.4)
Gastrooesophageal reflux disease	13 (5.4)	8 (3.4)
Haemorrhoids	1 (0.4)	1 (0.4)
Hiatus hernia	5 (2.1)	3 (1.3)
Inguinal hernia	3 (1.3)	4 (1.7)
Irritable bowel syndrome	2 (0.8)	0
Large intestine polyp	0	2 (0.9)
Mechanical ileus	0	1 (0.4)
Melaena	1 (0.4)	0
Nausea	9 (3.8)	9 (3.9)
Oesophagitis	0	4 (1.7)
Pancreatic cyst	0	1 (0.4)
Pancreatitis	1 (0.4)	0
Pancreatitis acute	1 (0.4)	0
Peptic ulcer	2 (0.8)	0
Proctitis ulcerative	1 (0.4)	0
Rectal haemorrhage	1 (0.4)	0
Retching	1 (0.4)	0
Small intestine ulcer	1 (0.4)	0
Umbilical hernia	0	1 (0.4)
Upper gastrointestinal haemorrhage	1 (0.4)	1 (0.4)
Varices oesophageal	0	1 (0.4)
Vomiting	2 (0.8)	5 (2.2)
General disorders and administration site conditions	11 (4.6)	11 (4.7)
Chest discomfort	0	1 (0.4)
Gait disturbance	0	1 (0.4)
Oedema peripheral	3 (1.3)	1 (0.4)
Pain	8 (3.3)	7 (3.0)
Pyrexia	0	1 (0.4)
Ulcer haemorrhage	0	1 (0.4)

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.4.1
Medical History
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Hepatobiliary disorders	16 (6.7)	20 (8.6)
Alcoholic liver disease	1 (0.4)	0
Autoimmune hepatitis	0	2 (0.9)
Bile duct stone	0	3 (1.3)
Cholecystitis	1 (0.4)	3 (1.3)
Cholelithiasis	5 (2.1)	2 (0.9)
Cholestasis	1 (0.4)	0
Cirrhosis alcoholic	1 (0.4)	0
Gallbladder disorder	0	1 (0.4)
Gallbladder rupture	1 (0.4)	0
Hepatic cirrhosis	2 (0.8)	2 (0.9)
Hepatic cyst	2 (0.8)	0
Hepatic failure	0	1 (0.4)
Hepatic steatosis	1 (0.4)	2 (0.9)
Hepatitis	1 (0.4)	0
Hepatosplenomegaly	0	1 (0.4)
Hyperbilirubinaemia	0	1 (0.4)
Liver disorder	1 (0.4)	2 (0.9)
Liver injury	0	2 (0.9)
Immune system disorders	6 (2.5)	2 (0.9)
Contrast media allergy	1 (0.4)	0
Graft versus host disease	1 (0.4)	0
Hypersensitivity	2 (0.8)	2 (0.9)
Multiple allergies	1 (0.4)	0
Seasonal allergy	1 (0.4)	0
Infections and infestations	31 (13.0)	27 (11.6)
Appendicitis	1 (0.4)	0
Bacteriuria	0	1 (0.4)
Bronchitis	1 (0.4)	0
COVID-19	4 (1.7)	6 (2.6)
COVID-19 pneumonia	0	1 (0.4)
Cellulitis	2 (0.8)	0
Chronic hepatitis C	0	2 (0.9)
Chronic sinusitis	1 (0.4)	0
Diverticulitis	1 (0.4)	0
Enterococcal infection	0	1 (0.4)
Erysipelas	2 (0.8)	0
Eye infection	1 (0.4)	0
Furuncle	0	1 (0.4)
Helicobacter infection	0	1 (0.4)
Hepatitis E	0	1 (0.4)
Herpes zoster	1 (0.4)	1 (0.4)
Infection	1 (0.4)	1 (0.4)
Influenza	1 (0.4)	0
Latent syphilis	0	1 (0.4)
Lyme disease	1 (0.4)	1 (0.4)
Mastoiditis	0	1 (0.4)
Pneumonia	5 (2.1)	3 (1.3)
Pneumonia aspiration	1 (0.4)	0
Prosthetic valve endocarditis	0	1 (0.4)
Pyelocystitis	1 (0.4)	0
Pyelonephritis acute	0	1 (0.4)
Rhinitis	0	1 (0.4)
Sepsis	1 (0.4)	0
Sinusitis	1 (0.4)	0
Syphilis	0	1 (0.4)
Urinary tract infection	8 (3.3)	2 (0.9)
Urosepsis	0	2 (0.9)

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Viral upper respiratory tract infection	1 (0.4)	0
Injury, poisoning and procedural complications	20 (8.4)	18 (7.8)
Ankle fracture	1 (0.4)	0
Arteriovenous fistula site pseudoaneurysm	1 (0.4)	0
Cataract operation complication	0	1 (0.4)
Chest injury	1 (0.4)	0
Contusion	1 (0.4)	2 (0.9)
Craniocerebral injury	1 (0.4)	0
Endotracheal intubation complication	1 (0.4)	0
Facial bones fracture	1 (0.4)	1 (0.4)
Fall	2 (0.8)	1 (0.4)
Femoral neck fracture	1 (0.4)	0
Femur fracture	1 (0.4)	1 (0.4)
Hand fracture	1 (0.4)	0
Hip fracture	1 (0.4)	0
Humerus fracture	1 (0.4)	0
Joint dislocation	1 (0.4)	0
Limb injury	2 (0.8)	0
Lower limb fracture	0	1 (0.4)
Lumbar vertebral fracture	1 (0.4)	1 (0.4)
Mouth injury	0	1 (0.4)
Multiple injuries	0	1 (0.4)
Pelvic fracture	1 (0.4)	0
Pneumoconiosis	0	1 (0.4)
Post laminectomy syndrome	1 (0.4)	0
Postoperative delirium	0	1 (0.4)
Radius fracture	2 (0.8)	1 (0.4)
Rib fracture	1 (0.4)	1 (0.4)
Silicosis	0	1 (0.4)
Skin laceration	0	1 (0.4)
Skull fractured base	1 (0.4)	0
Spinal compression fracture	0	1 (0.4)
Spinal fracture	0	2 (0.9)
Subdural haematoma	1 (0.4)	2 (0.9)
Upper limb fracture	1 (0.4)	0
Vascular access site ulcer	1 (0.4)	0
Vascular pseudoaneurysm	1 (0.4)	0
Wrist fracture	1 (0.4)	0
Investigations	10 (4.2)	12 (5.2)
Blood creatinine increased	0	1 (0.4)
Blood lactate dehydrogenase increased	0	1 (0.4)
Blood lactic acid increased	1 (0.4)	0
Blood uric acid increased	1 (0.4)	2 (0.9)
C-reactive protein increased	1 (0.4)	0
Cardiac murmur	1 (0.4)	1 (0.4)
Coagulation test abnormal	0	1 (0.4)
Endoscopic retrograde cholangiopancreatography	0	1 (0.4)
Fibrin D dimer increased	1 (0.4)	0
HIV test positive	0	2 (0.9)
Hepatic enzyme increased	2 (0.8)	1 (0.4)
Liver function test abnormal	0	1 (0.4)
Liver function test increased	1 (0.4)	0
Myocardial necrosis marker increased	1 (0.4)	0
Neutrophil count increased	0	1 (0.4)
Troponin increased	2 (0.8)	0
Metabolism and nutrition disorders	147 (61.5)	141 (60.8)
Diabetes mellitus	77 (32.2)	60 (25.9)
Dyslipidaemia	26 (10.9)	41 (17.7)

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Table 1.4.1
Medical History
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Folate deficiency	1 (0.4)	0
Glucose tolerance impaired	1 (0.4)	0
Gout	6 (2.5)	3 (1.3)
Hypercholesterolaemia	33 (13.8)	37 (15.9)
Hyperglycaemia	1 (0.4)	2 (0.9)
Hyperlipidaemia	30 (12.6)	30 (12.9)
Hypernatraemia	2 (0.8)	0
Hyperuricaemia	10 (4.2)	16 (6.9)
Hypochloraemia	1 (0.4)	0
Hypokalaemia	8 (3.3)	9 (3.9)
Hypomagnesaemia	0	2 (0.9)
Hyponatraemia	6 (2.5)	7 (3.0)
Hypoproteinaemia	0	1 (0.4)
Iodine deficiency	1 (0.4)	0
Iron deficiency	1 (0.4)	1 (0.4)
Lipid metabolism disorder	0	1 (0.4)
Obesity	10 (4.2)	12 (5.2)
Overweight	1 (0.4)	0
Vitamin B complex deficiency	1 (0.4)	0
Vitamin B12 deficiency	0	1 (0.4)
Vitamin D deficiency	6 (2.5)	1 (0.4)
Musculoskeletal and connective tissue disorders	63 (26.4)	62 (26.7)
Arthralgia	3 (1.3)	2 (0.9)
Arthritis	3 (1.3)	5 (2.2)
Arthropathy	1 (0.4)	0
Back pain	5 (2.1)	9 (3.9)
Bursitis	2 (0.8)	1 (0.4)
Dupuytren's contracture	0	1 (0.4)
Fibromyalgia	1 (0.4)	0
Flank pain	1 (0.4)	0
Gouty arthritis	0	1 (0.4)
Inclusion body myositis	1 (0.4)	0
Intervertebral disc degeneration	2 (0.8)	0
Intervertebral disc disorder	1 (0.4)	0
Intervertebral disc protrusion	3 (1.3)	1 (0.4)
Lumbar spinal stenosis	2 (0.8)	1 (0.4)
Muscle contracture	0	1 (0.4)
Muscle spasms	0	2 (0.9)
Musculoskeletal disorder	1 (0.4)	0
Myalgia	2 (0.8)	1 (0.4)
Neck pain	1 (0.4)	4 (1.7)
Osteoarthritis	17 (7.1)	9 (3.9)
Osteochondrosis	1 (0.4)	0
Osteonecrosis	0	1 (0.4)
Osteopenia	2 (0.8)	1 (0.4)
Osteoporosis	17 (7.1)	16 (6.9)
Osteoporosis postmenopausal	1 (0.4)	0
Pain in extremity	1 (0.4)	1 (0.4)
Polyarthritis	1 (0.4)	1 (0.4)
Polymyalgia rheumatica	5 (2.1)	3 (1.3)
Post-traumatic osteoporosis	0	1 (0.4)
Pseudarthrosis	1 (0.4)	0
Rheumatic fever	0	1 (0.4)
Rheumatoid arthritis	2 (0.8)	6 (2.6)
Rotator cuff syndrome	1 (0.4)	0
Spinal osteoarthritis	1 (0.4)	3 (1.3)
Spinal pain	1 (0.4)	1 (0.4)
Spinal stenosis	4 (1.7)	3 (1.3)
Spondylitis	0	1 (0.4)
Spondyloarthropathy	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Spondylolisthesis	1 (0.4)	0
Still's disease	0	1 (0.4)
Tendonitis	0	1 (0.4)
Tenosynovitis stenosans	0	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	59 (24.7)	64 (27.6)
Acanthoma	1 (0.4)	0
Adrenal adenoma	1 (0.4)	0
Basal cell carcinoma	1 (0.4)	0
Benign breast neoplasm	0	1 (0.4)
Benign neoplasm of prostate	0	1 (0.4)
Bladder cancer	0	1 (0.4)
Cardiac myxoma	1 (0.4)	0
Chondrosarcoma	0	1 (0.4)
Colorectal adenoma	3 (1.3)	0
Cutaneous T-cell lymphoma	0	1 (0.4)
Ependymoma	0	1 (0.4)
Essential thrombocythaemia	0	1 (0.4)
Haemangioma	1 (0.4)	0
Haemangioma of bone	0	1 (0.4)
Meningioma	0	1 (0.4)
Metastases to central nervous system	1 (0.4)	0
Neoplasm malignant	54 (22.6)	53 (22.8)
Neurofibroma	0	1 (0.4)
Pituitary tumour benign	1 (0.4)	1 (0.4)
Polycythaemia vera	3 (1.3)	0
Renal neoplasm	0	1 (0.4)
Sarcoma metastatic	1 (0.4)	0
Uterine leiomyoma	0	1 (0.4)
Nervous system disorders	110 (46.0)	110 (47.4)
Aphasia	1 (0.4)	0
Balance disorder	0	1 (0.4)
Basal ganglia haemorrhage	1 (0.4)	0
Bell's palsy	0	1 (0.4)
Brain oedema	1 (0.4)	0
Brain stem syndrome	0	1 (0.4)
Carotid arteriosclerosis	1 (0.4)	0
Carotid artery dissection	0	1 (0.4)
Carotid artery occlusion	1 (0.4)	0
Carotid artery stenosis	1 (0.4)	0
Cerebral amyloid angiopathy	0	1 (0.4)
Cerebral arteriosclerosis	0	1 (0.4)
Cerebral haemorrhage	0	2 (0.9)
Cerebral microangiopathy	0	1 (0.4)
Cerebrovascular accident	54 (22.6)	50 (21.6)
Cerebrovascular disorder	0	1 (0.4)
Cervicobrachial syndrome	1 (0.4)	0
Cognitive disorder	6 (2.5)	6 (2.6)
Dementia	13 (5.4)	13 (5.6)
Diabetic neuropathy	1 (0.4)	2 (0.9)
Dizziness	1 (0.4)	2 (0.9)
Dysarthria	0	2 (0.9)
Early infantile epileptic encephalopathy with burst-suppression	1 (0.4)	0
Epilepsy	10 (4.2)	11 (4.7)
Essential tremor	0	1 (0.4)
Facial paresis	1 (0.4)	0
Guillain-Barre syndrome	1 (0.4)	0
Headache	6 (2.5)	11 (4.7)

	Andexanet (N=239) n (%)	Usual Care (N=232) n (%)
Hemiparesis	1 (0.4)	2 (0.9)
Hemiplegia	0	1 (0.4)
Hepatic encephalopathy	0	1 (0.4)
Horner's syndrome	0	1 (0.4)
Hydrocephalus	1 (0.4)	1 (0.4)
Hyperkinesia	0	1 (0.4)
Hypertensive encephalopathy	0	1 (0.4)
Hypertonia	1 (0.4)	1 (0.4)
Intercostal neuralgia	1 (0.4)	0
Intracranial aneurysm	0	2 (0.9)
Lacunar infarction	0	1 (0.4)
Leukoencephalopathy	1 (0.4)	2 (0.9)
Migraine	2 (0.8)	0
Migraine without aura	0	1 (0.4)
Mixed dementia	0	1 (0.4)
Multiple sclerosis	1 (0.4)	0
Neuralgia	2 (0.8)	0
Neuritis	0	1 (0.4)
Neuropathy peripheral	2 (0.8)	1 (0.4)
Paraesthesia	0	1 (0.4)
Parkinson's disease	5 (2.1)	6 (2.6)
Parkinsonism	1 (0.4)	1 (0.4)
Partial seizures	0	2 (0.9)
Polyneuropathy	3 (1.3)	2 (0.9)
Post herpetic neuralgia	0	1 (0.4)
Pseudoradicular syndrome	0	1 (0.4)
Radiculopathy	1 (0.4)	0
Restless legs syndrome	2 (0.8)	2 (0.9)
Seizure	1 (0.4)	5 (2.2)
Sleep deficit	0	1 (0.4)
Subarachnoid haemorrhage	3 (1.3)	0
Syncope	4 (1.7)	2 (0.9)
Transient global amnesia	0	2 (0.9)
Transient ischaemic attack	25 (10.5)	23 (9.9)
Tremor	1 (0.4)	0
Vascular dementia	1 (0.4)	0
Vascular encephalopathy	0	1 (0.4)
White matter lesion	1 (0.4)	0
Pregnancy, puerperium and perinatal conditions	1 (0.4)	0
Chronic villitis of unknown etiology	1 (0.4)	0
Psychiatric disorders	51 (21.3)	49 (21.1)
Adjustment disorder	1 (0.4)	0
Agitation	1 (0.4)	0
Alcohol abuse	1 (0.4)	2 (0.9)
Alcohol use disorder	1 (0.4)	0
Alcoholism	1 (0.4)	1 (0.4)
Anxiety	6 (2.5)	7 (3.0)
Claustrophobia	0	1 (0.4)
Delirium	1 (0.4)	1 (0.4)
Depressed mood	1 (0.4)	1 (0.4)
Depression	25 (10.5)	24 (10.3)
Depressive symptom	1 (0.4)	0
Dissociative identity disorder	1 (0.4)	0
Drug abuse	1 (0.4)	0
Insomnia	8 (3.3)	12 (5.2)
Mental status changes	0	1 (0.4)
Mixed anxiety and depressive disorder	2 (0.8)	1 (0.4)
Nervousness	0	1 (0.4)
Panic disorder	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Persistent depressive disorder	1 (0.4)	0
Polydipsia psychogenic	1 (0.4)	0
Psychiatric decompensation	0	1 (0.4)
Restlessness	2 (0.8)	0
Sleep disorder	5 (2.1)	4 (1.7)
Somatic symptom disorder	1 (0.4)	0
Substance abuse	0	1 (0.4)
Tobacco abuse	1 (0.4)	1 (0.4)
Renal and urinary disorders	64 (26.8)	44 (19.0)
Acute kidney injury	1 (0.4)	6 (2.6)
Bladder dysfunction	0	2 (0.9)
Chronic kidney disease	36 (15.1)	32 (13.8)
Cystitis haemorrhagic	1 (0.4)	0
Hydronephrosis	0	1 (0.4)
Hypertonic bladder	3 (1.3)	0
Incontinence	1 (0.4)	1 (0.4)
Kidney small	0	1 (0.4)
Nephrolithiasis	5 (2.1)	1 (0.4)
Pollakiuria	1 (0.4)	0
Polyuria	1 (0.4)	0
Renal artery thrombosis	1 (0.4)	0
Renal cyst	1 (0.4)	1 (0.4)
Renal disorder	0	1 (0.4)
Renal failure	1 (0.4)	3 (1.3)
Renal impairment	1 (0.4)	0
Ureterolithiasis	0	1 (0.4)
Urethral stenosis	1 (0.4)	0
Urge incontinence	2 (0.8)	1 (0.4)
Urinary incontinence	10 (4.2)	0
Urinary retention	3 (1.3)	1 (0.4)
Urinary tract disorder	1 (0.4)	0
Reproductive system and breast disorders	42 (17.6)	32 (13.8)
Benign prostatic hyperplasia	37 (15.5)	31 (13.4)
Fibrocystic breast disease	2 (0.8)	0
Ovarian cyst	1 (0.4)	0
Prostatomegaly	1 (0.4)	0
Scrotal cyst	1 (0.4)	0
Vaginal prolapse	0	1 (0.4)
Vulvovaginal dryness	0	1 (0.4)
Respiratory, thoracic and mediastinal disorders	63 (26.4)	60 (25.9)
Asthma	10 (4.2)	5 (2.2)
Bronchitis chronic	0	1 (0.4)
Chronic obstructive pulmonary disease	18 (7.5)	19 (8.2)
Cough	1 (0.4)	1 (0.4)
Dyspnoea	1 (0.4)	3 (1.3)
Emphysema	1 (0.4)	0
Haemoptysis	1 (0.4)	0
Interstitial lung disease	1 (0.4)	2 (0.9)
Nasal polyps	0	1 (0.4)
Obstructive sleep apnoea syndrome	3 (1.3)	5 (2.2)
Pleural effusion	1 (0.4)	2 (0.9)
Pneumothorax	1 (0.4)	0
Productive cough	1 (0.4)	0
Pulmonary arterial hypertension	1 (0.4)	1 (0.4)
Pulmonary congestion	0	1 (0.4)
Pulmonary embolism	20 (8.4)	23 (9.9)
Pulmonary fibrosis	1 (0.4)	0
Pulmonary hypertension	3 (1.3)	4 (1.7)

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Pulmonary mass	3 (1.3)	2 (0.9)
Pulmonary venous hypertension	1 (0.4)	0
Respiratory failure	1 (0.4)	1 (0.4)
Rhinitis allergic	0	1 (0.4)
Sleep apnoea syndrome	5 (2.1)	5 (2.2)
Skin and subcutaneous tissue disorders	12 (5.0)	9 (3.9)
Actinic elastosis	1 (0.4)	0
Cutaneous amyloidosis	0	1 (0.4)
Dandruff	1 (0.4)	0
Dermatitis contact	0	1 (0.4)
Dry skin	0	1 (0.4)
Eczema	0	3 (1.3)
Livedo reticularis	0	1 (0.4)
Neurodermatitis	1 (0.4)	0
Pemphigoid	1 (0.4)	0
Pruritus	2 (0.8)	0
Psoriasis	2 (0.8)	1 (0.4)
Seborrhoeic dermatitis	2 (0.8)	0
Skin ulcer	1 (0.4)	2 (0.9)
Urticaria aquagenic	1 (0.4)	0
Urticaria chronic	1 (0.4)	0
Social circumstances	3 (1.3)	5 (2.2)
Cardiac valve prosthesis user	0	1 (0.4)
Familial risk factor	0	1 (0.4)
Joint prosthesis user	1 (0.4)	1 (0.4)
Menopause	2 (0.8)	0
Tobacco user	0	1 (0.4)
Vascular device user	0	1 (0.4)
Surgical and medical procedures	39 (16.3)	36 (15.5)
Annuloplasty	0	1 (0.4)
Aortic valve replacement	1 (0.4)	3 (1.3)
Appendicectomy	5 (2.1)	1 (0.4)
Arm amputation	1 (0.4)	0
Arthrodesis	0	1 (0.4)
Blepharoplasty	0	1 (0.4)
Cardiac ablation	1 (0.4)	0
Cardiac operation	1 (0.4)	0
Cardiac pacemaker insertion	8 (3.3)	5 (2.2)
Cardioversion	1 (0.4)	0
Cataract operation	2 (0.8)	1 (0.4)
Cholecystectomy	5 (2.1)	7 (3.0)
Coronary arterial stent insertion	0	3 (1.3)
Coronary artery bypass	0	1 (0.4)
Endarterectomy	0	1 (0.4)
Eye operation	0	1 (0.4)
Foot amputation	0	1 (0.4)
Foot operation	1 (0.4)	0
Gastric banding	0	1 (0.4)
Haemorrhoid operation	0	1 (0.4)
Hernia hiatus repair	1 (0.4)	0
Hip arthroplasty	5 (2.1)	2 (0.9)
Hip surgery	1 (0.4)	0
Hysterectomy	3 (1.3)	1 (0.4)
Implantable defibrillator insertion	1 (0.4)	1 (0.4)
Incisional hernia repair	0	1 (0.4)
Intraocular lens implant	1 (0.4)	2 (0.9)
Knee arthroplasty	2 (0.8)	1 (0.4)
Knee operation	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Leg amputation	1 (0.4)	1 (0.4)
Lens extraction	0	2 (0.9)
Liver transplant	0	2 (0.9)
Mammoplasty	0	1 (0.4)
Mastectomy	1 (0.4)	1 (0.4)
Mitral valve repair	2 (0.8)	0
Nephrectomy	3 (1.3)	0
Orchidectomy	1 (0.4)	0
Ovarian cystectomy	1 (0.4)	0
Pacemaker generated rhythm	1 (0.4)	0
Pancreatectomy	0	1 (0.4)
Parathyroidectomy	0	1 (0.4)
Peripheral endarterectomy	0	1 (0.4)
Polypectomy	2 (0.8)	0
Prostatectomy	1 (0.4)	1 (0.4)
Radioactive iodine therapy	1 (0.4)	0
Renal transplant	1 (0.4)	0
Sigmoidectomy	0	1 (0.4)
Small intestinal resection	1 (0.4)	0
Spinal fusion surgery	1 (0.4)	0
Splenectomy	1 (0.4)	0
Surgery	1 (0.4)	0
Thyroidectomy	1 (0.4)	2 (0.9)
Transcatheter aortic valve implantation	0	1 (0.4)
Umbilical hernia repair	0	2 (0.9)
Urinary tract operation	1 (0.4)	0
Varicocele repair	1 (0.4)	0
Vascular disorders	207 (86.6)	191 (82.3)
Aneurysm	1 (0.4)	0
Aortic aneurysm	2 (0.8)	0
Aortic dilatation	4 (1.7)	2 (0.9)
Aortic dissection	0	1 (0.4)
Aortic stenosis	3 (1.3)	1 (0.4)
Aortic thrombosis	0	1 (0.4)
Arteriosclerosis	3 (1.3)	1 (0.4)
Circulatory collapse	1 (0.4)	0
Deep vein thrombosis	18 (7.5)	26 (11.2)
Essential hypertension	4 (1.7)	3 (1.3)
Giant cell arteritis	0	1 (0.4)
Haematoma	1 (0.4)	0
Hypertension	194 (81.2)	184 (79.3)
Hypertensive crisis	1 (0.4)	1 (0.4)
Intermittent claudication	1 (0.4)	0
Lymphoedema	2 (0.8)	0
Microangiopathy	1 (0.4)	0
Peripheral arterial occlusive disease	1 (0.4)	4 (1.7)
Peripheral artery thrombosis	0	1 (0.4)
Peripheral vascular disorder	8 (3.3)	9 (3.9)
Peripheral venous disease	0	2 (0.9)
Varicose vein	4 (1.7)	0

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Overall	236	228
No comorbidities	3	4
Blood and lymphatic system disorders	18 (7.5)	20 (8.6)
Anaemia	8 (3.3)	10 (4.3)
Autoimmune haemolytic anaemia	0	1 (0.4)
Febrile neutropenia	1 (0.4)	0
Granulomatous lymphadenitis	0	1 (0.4)
Heparin-induced thrombocytopenia	0	1 (0.4)
Hypochromic anaemia	1 (0.4)	0
Iron deficiency anaemia	1 (0.4)	1 (0.4)
Leukocytosis	1 (0.4)	0
Lymphadenopathy mediastinal	1 (0.4)	1 (0.4)
Microcytic anaemia	1 (0.4)	0
Normochromic normocytic anaemia	1 (0.4)	0
Pancytopenia	0	1 (0.4)
Polycythaemia	0	1 (0.4)
Splenomegaly	0	2 (0.9)
Thrombocytopenia	3 (1.3)	4 (1.7)
Thrombocytosis	1 (0.4)	0
Cardiac disorders	214 (89.5)	206 (88.8)
Acute coronary syndrome	1 (0.4)	0
Angina pectoris	11 (4.6)	9 (3.9)
Angina unstable	3 (1.3)	0
Aortic valve incompetence	4 (1.7)	6 (2.6)
Aortic valve sclerosis	1 (0.4)	0
Aortic valve stenosis	2 (0.8)	1 (0.4)
Arrhythmia	0	1 (0.4)
Arteriosclerosis coronary artery	3 (1.3)	4 (1.7)
Atrial fibrillation	206 (86.2)	189 (81.5)
Atrial flutter	0	3 (1.3)
Atrioventricular block complete	3 (1.3)	0
Atrioventricular block first degree	3 (1.3)	3 (1.3)
Atrioventricular block second degree	1 (0.4)	1 (0.4)
Bradyarrhythmia	0	1 (0.4)
Bradycardia	2 (0.8)	5 (2.2)
Bundle branch block left	1 (0.4)	5 (2.2)
Bundle branch block right	1 (0.4)	4 (1.7)
Cardiac failure	0	3 (1.3)
Cardiac failure chronic	1 (0.4)	0
Cardiac failure congestive	31 (13.0)	45 (19.4)
Cardiac valve disease	0	1 (0.4)
Cardiomyopathy	1 (0.4)	2 (0.9)
Cardiovascular insufficiency	1 (0.4)	0
Coronary artery disease	10 (4.2)	19 (8.2)
Coronary artery insufficiency	1 (0.4)	0
Coronary artery occlusion	1 (0.4)	0
Coronary artery stenosis	1 (0.4)	0
Diastolic dysfunction	0	2 (0.9)
Hypertensive cardiomyopathy	1 (0.4)	1 (0.4)
Hypertensive heart disease	1 (0.4)	0
Ischaemic cardiomyopathy	0	1 (0.4)
Left atrial dilatation	0	1 (0.4)
Left ventricular hypertrophy	0	1 (0.4)
Mitral valve incompetence	6 (2.5)	4 (1.7)
Myocardial ischaemia	7 (2.9)	8 (3.4)
Palpitations	1 (0.4)	0
Pericardial cyst	1 (0.4)	0

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Pericardial effusion	0	1 (0.4)
Pericarditis	1 (0.4)	0
Sinus bradycardia	1 (0.4)	2 (0.9)
Sinus node dysfunction	4 (1.7)	3 (1.3)
Sinus tachycardia	0	2 (0.9)
Supraventricular tachycardia	2 (0.8)	1 (0.4)
Tachyarrhythmia	0	1 (0.4)
Tachycardia	0	1 (0.4)
Tricuspid valve incompetence	1 (0.4)	6 (2.6)
Ventricular tachycardia	1 (0.4)	0
Congenital, familial and genetic disorders	3 (1.3)	8 (3.4)
Atrial septal defect	0	3 (1.3)
Factor VII deficiency	0	1 (0.4)
Gilbert's syndrome	0	2 (0.9)
Heart disease congenital	1 (0.4)	0
Hypoplastic left heart syndrome	0	1 (0.4)
Muscular dystrophy	1 (0.4)	0
Syndactyly	1 (0.4)	1 (0.4)
Ear and labyrinth disorders	5 (2.1)	3 (1.3)
Ear haemorrhage	0	1 (0.4)
Hypoacusis	1 (0.4)	0
Meniere's disease	0	2 (0.9)
Presbyacusis	1 (0.4)	0
Vertigo	2 (0.8)	1 (0.4)
Vertigo positional	1 (0.4)	0
Endocrine disorders	52 (21.8)	55 (23.7)
Adrenal insufficiency	0	1 (0.4)
Autoimmune thyroiditis	0	1 (0.4)
Goitre	6 (2.5)	2 (0.9)
Hyperparathyroidism	1 (0.4)	0
Hyperparathyroidism secondary	0	1 (0.4)
Hyperthyroidism	8 (3.3)	8 (3.4)
Hypoparathyroidism	1 (0.4)	0
Hypothyroidism	35 (14.6)	41 (17.7)
Thyroid disorder	0	1 (0.4)
Thyroid mass	2 (0.8)	0
Eye disorders	26 (10.9)	16 (6.9)
Age-related macular degeneration	1 (0.4)	0
Blindness	2 (0.8)	0
Blindness unilateral	0	2 (0.9)
Cataract	3 (1.3)	3 (1.3)
Diabetic retinopathy	1 (0.4)	2 (0.9)
Dry age-related macular degeneration	0	1 (0.4)
Epiretinal membrane	1 (0.4)	0
Eye disorder	0	1 (0.4)
Glaucoma	12 (5.0)	6 (2.6)
Macular degeneration	2 (0.8)	0
Neovascular age-related macular degeneration	1 (0.4)	0
Ocular hypertension	1 (0.4)	1 (0.4)
Optic ischaemic neuropathy	0	1 (0.4)
Retinal detachment	1 (0.4)	0
Retinopathy	1 (0.4)	0
Retinopathy hypertensive	1 (0.4)	0
Vitreous haemorrhage	1 (0.4)	0
Gastrointestinal disorders	48 (20.1)	34 (14.7)
Abdominal distension	0	1 (0.4)

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Abdominal pain lower	0	1 (0.4)
Ascites	1 (0.4)	0
Barrett's oesophagus	2 (0.8)	1 (0.4)
Chronic gastritis	2 (0.8)	0
Coeliac disease	1 (0.4)	1 (0.4)
Colitis ischaemic	0	1 (0.4)
Colitis ulcerative	2 (0.8)	1 (0.4)
Constipation	8 (3.3)	7 (3.0)
Crohn's disease	4 (1.7)	0
Dental caries	0	1 (0.4)
Diaphragmatic hernia	1 (0.4)	0
Diverticulum	4 (1.7)	1 (0.4)
Diverticulum intestinal	3 (1.3)	2 (0.9)
Duodenal ulcer	0	1 (0.4)
Dyspepsia	4 (1.7)	0
Dysphagia	1 (0.4)	0
Gastric ulcer	1 (0.4)	0
Gastritis	3 (1.3)	2 (0.9)
Gastritis alcoholic	1 (0.4)	0
Gastrointestinal angiodysplasia	0	1 (0.4)
Gastrointestinal ulcer	1 (0.4)	1 (0.4)
Gastrooesophageal reflux disease	13 (5.4)	7 (3.0)
Haemorrhoids	1 (0.4)	1 (0.4)
Hiatus hernia	2 (0.8)	3 (1.3)
Inguinal hernia	3 (1.3)	1 (0.4)
Irritable bowel syndrome	2 (0.8)	0
Large intestine polyp	0	2 (0.9)
Nausea	3 (1.3)	4 (1.7)
Oesophagitis	0	1 (0.4)
Pancreatic cyst	0	1 (0.4)
Pancreatitis	1 (0.4)	0
Small intestine ulcer	1 (0.4)	0
Varices oesophageal	0	1 (0.4)
Vomiting	0	1 (0.4)
General disorders and administration site conditions	10 (4.2)	9 (3.9)
Chest discomfort	0	1 (0.4)
Gait disturbance	0	1 (0.4)
Oedema peripheral	3 (1.3)	1 (0.4)
Pain	7 (2.9)	7 (3.0)
Hepatobiliary disorders	13 (5.4)	14 (6.0)
Alcoholic liver disease	1 (0.4)	0
Autoimmune hepatitis	0	1 (0.4)
Bile duct stone	0	1 (0.4)
Cholecystitis	1 (0.4)	1 (0.4)
Cholelithiasis	3 (1.3)	0
Cholestasis	1 (0.4)	0
Cirrhosis alcoholic	1 (0.4)	0
Gallbladder disorder	0	1 (0.4)
Hepatic cirrhosis	2 (0.8)	1 (0.4)
Hepatic cyst	2 (0.8)	0
Hepatic failure	0	1 (0.4)
Hepatic steatosis	1 (0.4)	2 (0.9)
Hepatosplenomegaly	0	1 (0.4)
Hyperbilirubinaemia	0	1 (0.4)
Liver disorder	1 (0.4)	2 (0.9)
Liver injury	0	2 (0.9)
Immune system disorders	6 (2.5)	2 (0.9)
Contrast media allergy	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Graft versus host disease	1 (0.4)	0
Hypersensitivity	2 (0.8)	2 (0.9)
Multiple allergies	1 (0.4)	0
Seasonal allergy	1 (0.4)	0
Infections and infestations	17 (7.1)	10 (4.3)
Bacteriuria	0	1 (0.4)
COVID-19	2 (0.8)	1 (0.4)
Cellulitis	2 (0.8)	0
Chronic hepatitis C	0	2 (0.9)
Chronic sinusitis	1 (0.4)	0
Diverticulitis	1 (0.4)	0
Erysipelas	1 (0.4)	0
Eye infection	1 (0.4)	0
Furuncle	0	1 (0.4)
Herpes zoster	1 (0.4)	0
Infection	1 (0.4)	1 (0.4)
Latent syphilis	0	1 (0.4)
Pneumonia	2 (0.8)	0
Prosthetic valve endocarditis	0	1 (0.4)
Rhinitis	0	1 (0.4)
Sinusitis	1 (0.4)	0
Urinary tract infection	6 (2.5)	1 (0.4)
Injury, poisoning and procedural complications	13 (5.4)	8 (3.4)
Contusion	1 (0.4)	0
Facial bones fracture	1 (0.4)	1 (0.4)
Fall	2 (0.8)	1 (0.4)
Hand fracture	1 (0.4)	0
Joint dislocation	1 (0.4)	0
Limb injury	1 (0.4)	0
Lumbar vertebral fracture	1 (0.4)	0
Multiple injuries	0	1 (0.4)
Pelvic fracture	1 (0.4)	0
Pneumoconiosis	0	1 (0.4)
Post laminectomy syndrome	1 (0.4)	0
Radius fracture	1 (0.4)	0
Rib fracture	1 (0.4)	1 (0.4)
Silicosis	0	1 (0.4)
Skull fractured base	1 (0.4)	0
Spinal compression fracture	0	1 (0.4)
Spinal fracture	0	1 (0.4)
Subdural haematoma	1 (0.4)	0
Vascular access site ulcer	1 (0.4)	0
Vascular pseudoaneurysm	1 (0.4)	0
Wrist fracture	1 (0.4)	0
Investigations	9 (3.8)	10 (4.3)
Blood creatinine increased	0	1 (0.4)
Blood lactate dehydrogenase increased	0	1 (0.4)
Blood uric acid increased	1 (0.4)	1 (0.4)
C-reactive protein increased	1 (0.4)	0
Cardiac murmur	1 (0.4)	1 (0.4)
Coagulation test abnormal	0	1 (0.4)
Fibrin D dimer increased	1 (0.4)	0
HIV test positive	0	2 (0.9)
Hepatic enzyme increased	2 (0.8)	1 (0.4)
Liver function test abnormal	0	1 (0.4)
Liver function test increased	1 (0.4)	0
Neutrophil count increased	0	1 (0.4)
Troponin increased	2 (0.8)	0

Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Metabolism and nutrition disorders	143 (59.8)	137 (59.1)
Diabetes mellitus	76 (31.8)	60 (25.9)
Dyslipidaemia	25 (10.5)	40 (17.2)
Folate deficiency	1 (0.4)	0
Glucose tolerance impaired	1 (0.4)	0
Gout	5 (2.1)	2 (0.9)
Hypercholesterolaemia	33 (13.8)	37 (15.9)
Hyperglycaemia	1 (0.4)	2 (0.9)
Hyperlipidaemia	29 (12.1)	30 (12.9)
Hypernatraemia	1 (0.4)	0
Hyperuricaemia	10 (4.2)	16 (6.9)
Hypochloraemia	1 (0.4)	0
Hypokalaemia	5 (2.1)	7 (3.0)
Hypomagnesaemia	0	2 (0.9)
Hyponatraemia	4 (1.7)	3 (1.3)
Hypoproteinaemia	0	1 (0.4)
Iodine deficiency	1 (0.4)	0
Iron deficiency	0	1 (0.4)
Lipid metabolism disorder	0	1 (0.4)
Obesity	10 (4.2)	11 (4.7)
Overweight	1 (0.4)	0
Vitamin B complex deficiency	1 (0.4)	0
Vitamin B12 deficiency	0	1 (0.4)
Vitamin D deficiency	6 (2.5)	1 (0.4)
Musculoskeletal and connective tissue disorders	61 (25.5)	57 (24.6)
Arthralgia	2 (0.8)	2 (0.9)
Arthritis	3 (1.3)	3 (1.3)
Arthropathy	1 (0.4)	0
Back pain	5 (2.1)	9 (3.9)
Bursitis	2 (0.8)	1 (0.4)
Dupuytren's contracture	0	1 (0.4)
Fibromyalgia	1 (0.4)	0
Gouty arthritis	0	1 (0.4)
Inclusion body myositis	1 (0.4)	0
Intervertebral disc degeneration	2 (0.8)	0
Intervertebral disc disorder	1 (0.4)	0
Intervertebral disc protrusion	2 (0.8)	1 (0.4)
Lumbar spinal stenosis	2 (0.8)	1 (0.4)
Muscle contracture	0	1 (0.4)
Muscle spasms	0	2 (0.9)
Musculoskeletal disorder	1 (0.4)	0
Myalgia	2 (0.8)	1 (0.4)
Neck pain	1 (0.4)	4 (1.7)
Osteoarthritis	17 (7.1)	8 (3.4)
Osteochondrosis	1 (0.4)	0
Osteonecrosis	0	1 (0.4)
Osteopenia	2 (0.8)	1 (0.4)
Osteoporosis	17 (7.1)	15 (6.5)
Osteoporosis postmenopausal	1 (0.4)	0
Pain in extremity	1 (0.4)	1 (0.4)
Polyarthritis	1 (0.4)	1 (0.4)
Polymyalgia rheumatica	5 (2.1)	3 (1.3)
Post-traumatic osteoporosis	0	1 (0.4)
Rheumatoid arthritis	2 (0.8)	6 (2.6)
Rotator cuff syndrome	1 (0.4)	0
Spinal osteoarthritis	1 (0.4)	3 (1.3)
Spinal stenosis	4 (1.7)	3 (1.3)
Spondylitis	0	1 (0.4)
Spondyloarthropathy	1 (0.4)	0

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Spondylolisthesis	1 (0.4)	0
Still's disease	0	1 (0.4)
Tendonitis	0	1 (0.4)
Tenosynovitis stenosans	0	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	24 (10.0)	30 (12.9)
Benign breast neoplasm	0	1 (0.4)
Chondrosarcoma	0	1 (0.4)
Colorectal adenoma	2 (0.8)	0
Cutaneous T-cell lymphoma	0	1 (0.4)
Essential thrombocythaemia	0	1 (0.4)
Haemangioma	1 (0.4)	0
Haemangioma of bone	0	1 (0.4)
Neoplasm malignant	18 (7.5)	23 (9.9)
Pituitary tumour benign	1 (0.4)	1 (0.4)
Polycythaemia vera	3 (1.3)	0
Renal neoplasm	0	1 (0.4)
Sarcoma metastatic	1 (0.4)	0
Nervous system disorders	59 (24.7)	61 (26.3)
Aphasia	1 (0.4)	0
Balance disorder	0	1 (0.4)
Basal ganglia haemorrhage	1 (0.4)	0
Bell's palsy	0	1 (0.4)
Brain oedema	1 (0.4)	0
Brain stem syndrome	0	1 (0.4)
Carotid arteriosclerosis	1 (0.4)	0
Carotid artery dissection	0	1 (0.4)
Carotid artery occlusion	1 (0.4)	0
Carotid artery stenosis	1 (0.4)	0
Cerebral amyloid angiopathy	0	1 (0.4)
Cerebral arteriosclerosis	0	1 (0.4)
Cerebral microangiopathy	0	1 (0.4)
Cerebrovascular accident	6 (2.5)	5 (2.2)
Cerebrovascular disorder	0	1 (0.4)
Cervicobrachial syndrome	1 (0.4)	0
Cognitive disorder	6 (2.5)	6 (2.6)
Dementia	13 (5.4)	13 (5.6)
Diabetic neuropathy	1 (0.4)	2 (0.9)
Dizziness	1 (0.4)	1 (0.4)
Dysarthria	0	1 (0.4)
Early infantile epileptic encephalopathy with burst-suppression	1 (0.4)	0
Epilepsy	7 (2.9)	9 (3.9)
Essential tremor	0	1 (0.4)
Headache	5 (2.1)	8 (3.4)
Hemiparesis	1 (0.4)	1 (0.4)
Hemiplegia	0	1 (0.4)
Horner's syndrome	0	1 (0.4)
Hyperkinesia	0	1 (0.4)
Hypertensive encephalopathy	0	1 (0.4)
Hypertonia	1 (0.4)	1 (0.4)
Intercostal neuralgia	1 (0.4)	0
Intracranial aneurysm	0	1 (0.4)
Lacunar infarction	0	1 (0.4)
Leukoencephalopathy	1 (0.4)	2 (0.9)
Migraine	2 (0.8)	0
Migraine without aura	0	1 (0.4)
Mixed dementia	0	1 (0.4)
Multiple sclerosis	1 (0.4)	0

Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Neuralgia	2 (0.8)	0
Neuritis	0	1 (0.4)
Neuropathy peripheral	2 (0.8)	1 (0.4)
Paraesthesia	0	1 (0.4)
Parkinson's disease	5 (2.1)	6 (2.6)
Parkinsonism	1 (0.4)	1 (0.4)
Partial seizures	0	1 (0.4)
Polyneuropathy	3 (1.3)	2 (0.9)
Post herpetic neuralgia	0	1 (0.4)
Pseudoradicular syndrome	0	1 (0.4)
Restless legs syndrome	2 (0.8)	2 (0.9)
Seizure	1 (0.4)	1 (0.4)
Sleep deficit	0	1 (0.4)
Syncope	1 (0.4)	0
Tremor	1 (0.4)	0
Vascular dementia	1 (0.4)	0
Vascular encephalopathy	0	1 (0.4)
White matter lesion	1 (0.4)	0
Pregnancy, puerperium and perinatal conditions	1 (0.4)	0
Chronic villitis of unknown etiology	1 (0.4)	0
Psychiatric disorders	49 (20.5)	47 (20.3)
Adjustment disorder	1 (0.4)	0
Agitation	1 (0.4)	0
Alcohol abuse	1 (0.4)	2 (0.9)
Alcohol use disorder	1 (0.4)	0
Alcoholism	0	1 (0.4)
Anxiety	6 (2.5)	7 (3.0)
Claustrophobia	0	1 (0.4)
Delirium	1 (0.4)	1 (0.4)
Depressed mood	1 (0.4)	1 (0.4)
Depression	24 (10.0)	24 (10.3)
Depressive symptom	1 (0.4)	0
Dissociative identity disorder	1 (0.4)	0
Drug abuse	1 (0.4)	0
Insomnia	7 (2.9)	11 (4.7)
Mixed anxiety and depressive disorder	2 (0.8)	1 (0.4)
Nervousness	0	1 (0.4)
Panic disorder	1 (0.4)	0
Persistent depressive disorder	1 (0.4)	0
Polydipsia psychogenic	1 (0.4)	0
Psychiatric decompensation	0	1 (0.4)
Restlessness	2 (0.8)	0
Sleep disorder	5 (2.1)	4 (1.7)
Somatic symptom disorder	1 (0.4)	0
Substance abuse	0	1 (0.4)
Tobacco abuse	1 (0.4)	0
Renal and urinary disorders	56 (23.4)	41 (17.7)
Acute kidney injury	0	2 (0.9)
Bladder dysfunction	0	2 (0.9)
Chronic kidney disease	34 (14.2)	32 (13.8)
Cystitis haemorrhagic	1 (0.4)	0
Hydronephrosis	0	1 (0.4)
Hypertonic bladder	3 (1.3)	0
Incontinence	1 (0.4)	1 (0.4)
Kidney small	0	1 (0.4)
Nephrolithiasis	2 (0.8)	1 (0.4)
Pollakiuria	1 (0.4)	0
Polyuria	1 (0.4)	0

Table 1.4.2
Comorbidities
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Renal artery thrombosis	1 (0.4)	0
Renal cyst	1 (0.4)	1 (0.4)
Renal disorder	0	1 (0.4)
Renal failure	1 (0.4)	3 (1.3)
Ureterolithiasis	0	1 (0.4)
Urethral stenosis	1 (0.4)	0
Urge incontinence	1 (0.4)	1 (0.4)
Urinary incontinence	9 (3.8)	0
Urinary retention	3 (1.3)	0
Urinary tract disorder	1 (0.4)	0
Reproductive system and breast disorders	37 (15.5)	31 (13.4)
Benign prostatic hyperplasia	33 (13.8)	30 (12.9)
Fibrocystic breast disease	1 (0.4)	0
Ovarian cyst	1 (0.4)	0
Prostatomegaly	1 (0.4)	0
Scrotal cyst	1 (0.4)	0
Vulvovaginal dryness	0	1 (0.4)
Respiratory, thoracic and mediastinal disorders	40 (16.7)	41 (17.7)
Asthma	9 (3.8)	5 (2.2)
Bronchitis chronic	0	1 (0.4)
Chronic obstructive pulmonary disease	17 (7.1)	19 (8.2)
Cough	1 (0.4)	1 (0.4)
Dyspnoea	1 (0.4)	2 (0.9)
Emphysema	1 (0.4)	0
Interstitial lung disease	1 (0.4)	2 (0.9)
Nasal polyps	0	1 (0.4)
Obstructive sleep apnoea syndrome	3 (1.3)	5 (2.2)
Productive cough	1 (0.4)	0
Pulmonary arterial hypertension	0	1 (0.4)
Pulmonary congestion	0	1 (0.4)
Pulmonary embolism	0	2 (0.9)
Pulmonary fibrosis	1 (0.4)	0
Pulmonary hypertension	3 (1.3)	4 (1.7)
Pulmonary mass	3 (1.3)	2 (0.9)
Pulmonary venous hypertension	1 (0.4)	0
Respiratory failure	1 (0.4)	0
Rhinitis allergic	0	1 (0.4)
Sleep apnoea syndrome	5 (2.1)	5 (2.2)
Skin and subcutaneous tissue disorders	12 (5.0)	7 (3.0)
Actinic elastosis	1 (0.4)	0
Cutaneous amyloidosis	0	1 (0.4)
Dandruff	1 (0.4)	0
Dermatitis contact	0	1 (0.4)
Eczema	0	3 (1.3)
Neurodermatitis	1 (0.4)	0
Pemphigoid	1 (0.4)	0
Pruritus	2 (0.8)	0
Psoriasis	2 (0.8)	0
Seborrhoeic dermatitis	2 (0.8)	0
Skin ulcer	1 (0.4)	2 (0.9)
Urticaria aquagenic	1 (0.4)	0
Urticaria chronic	1 (0.4)	0
Social circumstances	3 (1.3)	3 (1.3)
Joint prosthesis user	1 (0.4)	1 (0.4)
Menopause	2 (0.8)	0
Tobacco user	0	1 (0.4)
Vascular device user	0	1 (0.4)

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Surgical and medical procedures	13 (5.4)	14 (6.0)
Aortic valve replacement	0	2 (0.9)
Appendicectomy	1 (0.4)	0
Arm amputation	1 (0.4)	0
Arthrodesis	0	1 (0.4)
Cardiac pacemaker insertion	6 (2.5)	2 (0.9)
Cataract operation	0	1 (0.4)
Coronary arterial stent insertion	0	2 (0.9)
Coronary artery bypass	0	1 (0.4)
Foot operation	1 (0.4)	0
Hip arthroplasty	2 (0.8)	1 (0.4)
Hysterectomy	2 (0.8)	0
Implantable defibrillator insertion	1 (0.4)	1 (0.4)
Intraocular lens implant	0	1 (0.4)
Knee arthroplasty	0	1 (0.4)
Leg amputation	1 (0.4)	1 (0.4)
Pacemaker generated rhythm	1 (0.4)	0
Parathyroidectomy	0	1 (0.4)
Radioactive iodine therapy	1 (0.4)	0
Spinal fusion surgery	1 (0.4)	0
Vascular disorders	199 (83.3)	185 (79.7)
Aneurysm	1 (0.4)	0
Aortic aneurysm	2 (0.8)	0
Aortic dilatation	2 (0.8)	2 (0.9)
Aortic stenosis	3 (1.3)	1 (0.4)
Arteriosclerosis	3 (1.3)	1 (0.4)
Deep vein thrombosis	2 (0.8)	4 (1.7)
Essential hypertension	4 (1.7)	3 (1.3)
Haematoma	1 (0.4)	0
Hypertension	191 (79.9)	181 (78.0)
Hypertensive crisis	1 (0.4)	1 (0.4)
Lymphoedema	1 (0.4)	0
Microangiopathy	1 (0.4)	0
Peripheral arterial occlusive disease	1 (0.4)	4 (1.7)
Peripheral vascular disorder	7 (2.9)	7 (3.0)
Peripheral venous disease	0	2 (0.9)
Varicose vein	4 (1.7)	0

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Table 1.5
Summary of Randomized and Received Treatment
Intent-To-Treat Set

	Total (N=474)
	n (%)
Randomized to Andexanet	241
Received Andexanet High	51 (21.2)
Received Andexanet Low	185 (76.8)
Received Usual Care	2 (0.8)
Received No Treatment	3 (1.2)
Randomized to Usual Care	233
Received PCC	204 (87.6)
Received Other Therapy	2 (0.9)
Received No Treatment	24 (10.3)
Received Andexanet High	1 (0.4)
Received Andexanet Low	2 (0.9)

Table 1.6.1
Observation Duration for Efficacy Endpoints
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)
Study duration (Days)	n (missing)	241 (0)	233 (0)
	Mean (SD)	28.0 (12.81)	28.6 (13.45)
	Median	31.0	32.0
	Q1, Q3	21.0, 36.0	26.0, 35.0
	Min, Max	1, 80	1, 102
Effective hemostasis 12 hours post-randomization Follow-up duration (Hours)	n (missing)	231 (10)	228 (5)
	Mean (SD)	11.7 (1.33)	11.8 (1.29)
	Median	11.9	11.9
	Q1, Q3	11.3, 12.2	11.4, 12.1
	Min, Max	0, 17	2, 23
Anti-FXa Activity Follow-up duration (Hours)	n (missing)	229 (12)	225 (8)
	Mean (SD)	2.1 (0.44)	2.0 (0.41)
	Median	2.1	2.0
	Q1, Q3	2.0, 2.2	1.9, 2.2
	Min, Max	1, 4	0, 4
Total Score NIHSS Follow-up duration (Hours)	n (missing)	232 (9)	231 (2)
	Mean (SD)	49.0 (28.68)	48.9 (28.74)
	Median	69.5	70.0
	Q1, Q3	12.4, 72.1	12.2, 72.1
	Min, Max	2, 89	2, 85
GCS01-Total Score Follow-up duration (Hours)	n (missing)	166 (75)	159 (74)
	Mean (SD)	63.9 (19.82)	67.0 (15.77)
	Median	71.7	71.8
	Q1, Q3	69.1, 72.4	70.2, 72.6
	Min, Max	0, 81	2, 85
MRS01-Modified Rankin Scale Score Follow-up duration (Days)	n (missing)	237 (4)	229 (4)
	Mean (SD)	23.4 (16.77)	24.6 (16.23)
	Median	31.0	32.0
	Q1, Q3	1.0, 35.0	1.0, 34.0
	Min, Max	1, 80	1, 102
Endogenous Thrombin Potential (nM x min) Follow-up duration (Hours)	n (missing)	214 (27)	197 (36)
	Mean (SD)	11.0 (3.58)	10.8 (3.56)
	Median	12.0	11.9
	Q1, Q3	11.5, 12.4	11.2, 12.2
	Min, Max	0, 20	0, 21
ETP Lag Time (minutes) Follow-up duration (Hours)	n (missing)	215 (26)	209 (24)
	Mean (SD)	11.1 (3.50)	10.9 (3.43)
	Median	12.0	11.9
	Q1, Q3	11.5, 12.4	11.2, 12.2
	Min, Max	0, 20	0, 21

Study duration calculated as time from randomization until study completion or discontinuation.
Effective hemostasis follow-up calculated as time from randomization until minimum of: time of death in first 15 hours post-randomization, 12 hour visit of NIHSS or 12 hour CT scan/MRI.
Anti-FXa Activity, NIHSS, GCS, mRs: Follow-up calculated as time from randomization until last non-missing assessment.
If no valid date/time available, participents are set as 'Missing'

Table 1.6.1
Observation Duration for Efficacy Endpoints
Intent-To-Treat Set

		Andexanet (N=241)	Usual Care (N=233)
ETP Peak Height (nM) Follow-up duration (Hours)	n (missing)	215 (26)	209 (24)
	Mean (SD)	11.1 (3.50)	10.9 (3.43)
	Median	12.0	11.9
	Q1, Q3	11.5, 12.4	11.2, 12.2
	Min, Max	0, 20	0, 21
ETP Time to Peak (minutes) Follow-up duration (Hours)	n (missing)	215 (26)	209 (24)
	Mean (SD)	11.1 (3.50)	10.9 (3.43)
	Median	12.0	11.9
	Q1, Q3	11.5, 12.4	11.2, 12.2
	Min, Max	0, 20	0, 21
ETP Velocity Index (nM/min) Follow-up duration (Hours)	n (missing)	215 (26)	209 (24)
	Mean (SD)	11.1 (3.50)	10.9 (3.43)
	Median	12.0	11.9
	Q1, Q3	11.5, 12.4	11.2, 12.2
	Min, Max	0, 20	0, 21

Study duration calculated as time from randomization until study completion or discontinuation.
Effective hemostasis follow-up calculated as time from randomization until minimum of: time of death in first 15 hours post-randomization, 12 hour visit of NIHSS or 12 hour CT scan/MRI.
Anti-FXa Activity, NIHSS, GCS, mRs: Follow-up calculated as time from randomization until last non-missing assessment.
If no valid date/time available, participents are set as 'Missing'

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Table 1.6.2
Observation Duration for Safety Endpoints
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
Overall Survival Follow-up duration (Days)	n (missing)	239 (0)	232 (0)
	Mean (SD)	26.2 (10.99)	26.0 (11.07)
	Median	30.1	30.4
	Q1, Q3	20.2, 34.1	22.7, 33.2
	Min, Max	0, 37	0, 37
Adverse Events Follow-up duration (Days)	n (missing)	239 (0)	232 (0)
	Mean (SD)	28.3 (12.57)	28.4 (13.53)
	Median	32.0	32.0
	Q1, Q3	22.0, 36.0	24.0, 35.0
	Min, Max	1, 80	1, 102
Overall Treatment duration (Hours)	n (missing)	238 (1)	183 (49)
	Mean (SD)	136.6 (13.23)	46.6 (94.18)
	Median	135.0	30.0
	Q1, Q3	135.0, 139.0	15.0, 60.0
	Min, Max	40, 178	1, 1200

Overall Survival follow-up calculated as time from randomization until minimum of: (Maximum of study end, treatment end or randomization) or randomization + 37 days.
Adverse Events follow-up calculated as time from treatment start until minimum of: Treatment end or study end.
Treatment duration for Andexanet calculated as Overall Initial IV Bolus and IV Infusion Duration.
If no valid date/time available, participents are set as 'Missing'

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Table 2.1.1
Proportion of Participants With Effective Hemostasis Assessed at 12 Hours Post-Randomization
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	151/241 (62.7)	122/233 (52.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.19 (1.02, 1.39)	
p-value	0.0254	
Odds Ratio (95% CI)	1.53 (1.06, 2.22)	
p-value	0.0245	
Risk Difference (95% CI)	10.08 (1.35, 18.82)	
p-value	0.0236	
p-value of CMH-Test	0.0244	
p-value of Breslow-Day Test	0.4678	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.1.1
Proportion of Participants With Effective Hemostasis Assessed at 12 Hours Post-Randomization - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.9748
<65 years	10/ 13 (76.9)	10/ 16 (62.5)	1.18 (0.74, 1.88)	0.4863	
65 - 74 years	25/ 45 (55.6)	22/ 51 (43.1)	1.25 (0.82, 1.90)	0.3040	
>=75 years	116/ 183 (63.4)	90/ 166 (54.2)	1.18 (0.99, 1.41)	0.0605	
Sex					0.2539
Male	80/ 130 (61.5)	55/ 118 (46.6)	1.31 (1.04, 1.66)	0.0224	
Female	71/ 111 (64.0)	67/ 115 (58.3)	1.10 (0.89, 1.34)	0.3800	
Race					0.4977
White	138/ 217 (63.6)	114/ 213 (53.5)	1.18 (1.01, 1.39)	0.0360	
Other	7/ 15 (46.7)	8/ 16 (50.0)	0.92 (0.44, 1.89)	0.8112	
Geographic Region 1					0.3279
North America	15/ 29 (51.7)	14/ 27 (51.9)	0.96 (0.59, 1.54)	0.8528	
Europe	136/ 212 (64.2)	108/ 206 (52.4)	1.23 (1.04, 1.44)	0.0128	
Prior FXa Inhibitor					0.3439
Apixaban	110/ 162 (67.9)	86/ 158 (54.4)	1.25 (1.05, 1.49)	0.0129	
Rivaroxaban	41/ 79 (51.9)	36/ 75 (48.0)	1.05 (0.77, 1.44)	0.7470	
Indication for prior FXa Inhibitor 1					0.3373
Atrial Fibrillation/Flutter	132/ 208 (63.5)	101/ 194 (52.1)	1.21 (1.02, 1.43)	0.0261	
Venous Thromboembolism	11/ 20 (55.0)	19/ 31 (61.3)	0.94 (0.58, 1.51)	0.7933	
Other	8/ 13 (61.5)	2/ 8 (25.0)	2.40 (0.68, 8.46)	0.1731	
Indication for prior FXa Inhibitor 2					0.6478
Atrial Fibrillation/Flutter	132/ 208 (63.5)	101/ 194 (52.1)	1.21 (1.02, 1.43)	0.0261	
Other	19/ 33 (57.6)	21/ 39 (53.8)	1.09 (0.72, 1.64)	0.6784	
Baseline Anti-FXa Activity 1					0.2228
<30 ng/mL	8/ 15 (53.3)	7/ 11 (63.6)	0.84 (0.43, 1.63)	0.5998	
>=30 ng/mL	133/ 211 (63.0)	99/ 202 (49.0)	1.28 (1.08, 1.53)	0.0041	
Baseline Anti-FXa Activity 2					0.8567
<75 ng/mL	46/ 67 (68.7)	28/ 52 (53.8)	1.28 (0.95, 1.71)	0.1076	
>=75 ng/mL	95/ 159 (59.7)	78/ 161 (48.4)	1.23 (1.01, 1.51)	0.0400	
ICH Score at baseline					0.4118
< 3	129/ 203 (63.5)	111/ 204 (54.4)	1.17 (1.00, 1.37)	0.0573	
>= 3	22/ 38 (57.9)	11/ 29 (37.9)	1.48 (0.86, 2.57)	0.1572	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.1.1
Proportion of Participants With Effective Hemostasis Assessed at 12 Hours Post-Randomization - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.6231
<30 mL	128/ 190 (67.4)	109/ 193 (56.5)	1.19 (1.02, 1.39)	0.0311	
>=30 mL	23/ 51 (45.1)	13/ 39 (33.3)	1.36 (0.80, 2.32)	0.2519	
Baseline Volume of Hematoma 2					0.8386
<0.5 mL	5/ 7 (71.4)	8/ 11 (72.7)	1.15 (0.73, 1.81)	0.5446	
>=0.5 mL	146/ 234 (62.4)	114/ 221 (51.6)	1.21 (1.03, 1.42)	0.0188	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	132/ 215 (61.4)	112/ 218 (51.4)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	0/ 1 (0.0)			
Intracranial - subdural	9/ 13 (69.2)	4/ 5 (80.0)			
Intracranial - subarachnoid	9/ 10 (90.0)	6/ 8 (75.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.3352
<8 hours	52/ 101 (51.5)	48/ 103 (46.6)	1.09 (0.82, 1.43)	0.5618	
>=8 hours	96/ 133 (72.2)	74/ 130 (56.9)	1.28 (1.06, 1.54)	0.0088	
Intended Usual Care Agent					0.1502
PCC	88/ 160 (55.0)	72/ 156 (46.2)	1.20 (0.96, 1.49)	0.1087	
Other	14/ 18 (77.8)	10/ 11 (90.9)	0.86 (0.63, 1.18)	0.3566	
Unknown	49/ 63 (77.8)	40/ 66 (60.6)	1.25 (0.99, 1.56)	0.0566	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.1
Effective Hemostasis: No increase in hematoma volume >35% (Assessed at 12 Hours Post-Randomization)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	171/241 (71.0)	135/233 (57.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.22 (1.07, 1.39)	
p-value	0.0035	
Odds Ratio (95% CI)	1.79 (1.22, 2.64)	
p-value	0.0032	
Risk Difference (95% CI)	12.78 (4.39, 21.18)	
p-value	0.0028	
p-value of CMH-Test	0.0031	
p-value of Breslow-Day Test	0.3575	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.1.1
Effective Hemostasis: No increase in hematoma volume >35% (Assessed at 12 Hours Post-Randomization) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.8488
<65 years	10/ 13 (76.9)	11/ 16 (68.8)	1.09 (0.70, 1.69)	0.7121	
65 - 74 years	30/ 45 (66.7)	26/ 51 (51.0)	1.27 (0.91, 1.78)	0.1664	
>=75 years	131/ 183 (71.6)	98/ 166 (59.0)	1.23 (1.05, 1.43)	0.0087	
Sex					0.5720
Male	89/ 130 (68.5)	63/ 118 (53.4)	1.27 (1.04, 1.55)	0.0185	
Female	82/ 111 (73.9)	72/ 115 (62.6)	1.18 (0.99, 1.41)	0.0687	
Race					0.9922
White	156/ 217 (71.9)	127/ 213 (59.6)	1.20 (1.05, 1.37)	0.0077	
Other	9/ 15 (60.0)	8/ 16 (50.0)	1.20 (0.64, 2.27)	0.5632	
Geographic Region 1					0.4201
North America	18/ 29 (62.1)	15/ 27 (55.6)	1.04 (0.69, 1.57)	0.8521	
Europe	153/ 212 (72.2)	120/ 206 (58.3)	1.24 (1.08, 1.43)	0.0024	
Prior FXa Inhibitor					0.5151
Apixaban	122/ 162 (75.3)	95/ 158 (60.1)	1.26 (1.08, 1.46)	0.0035	
Rivaroxaban	49/ 79 (62.0)	40/ 75 (53.3)	1.13 (0.87, 1.48)	0.3513	
Indication for prior FXa Inhibitor 1					0.1285
Atrial Fibrillation/Flutter	150/ 208 (72.1)	112/ 194 (57.7)	1.24 (1.07, 1.43)	0.0035	
Venous Thromboembolism	11/ 20 (55.0)	21/ 31 (67.7)	0.88 (0.55, 1.39)	0.5738	
Other	10/ 13 (76.9)	2/ 8 (25.0)	3.00 (0.88, 10.17)	0.0778	
Indication for prior FXa Inhibitor 2					0.5888
Atrial Fibrillation/Flutter	150/ 208 (72.1)	112/ 194 (57.7)	1.24 (1.07, 1.43)	0.0035	
Other	21/ 33 (63.6)	23/ 39 (59.0)	1.11 (0.78, 1.60)	0.5585	
Baseline Anti-FXa Activity 1					0.2255
<30 ng/mL	10/ 15 (66.7)	8/ 11 (72.7)	0.92 (0.54, 1.57)	0.7623	
>=30 ng/mL	149/ 211 (70.6)	110/ 202 (54.5)	1.30 (1.11, 1.51)	0.0007	
Baseline Anti-FXa Activity 2					0.6463
<75 ng/mL	51/ 67 (76.1)	33/ 52 (63.5)	1.20 (0.94, 1.53)	0.1425	
>=75 ng/mL	108/ 159 (67.9)	85/ 161 (52.8)	1.29 (1.08, 1.54)	0.0053	
ICH Score at baseline					0.4135
< 3	142/ 203 (70.0)	120/ 204 (58.8)	1.19 (1.03, 1.38)	0.0181	
>= 3	29/ 38 (76.3)	15/ 29 (51.7)	1.43 (0.95, 2.16)	0.0904	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.1.1
Effective Hemostasis: No increase in hematoma volume >35% (Assessed at 12 Hours Post-Randomization) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.5408
<30 mL	139/ 190 (73.2)	117/ 193 (60.6)	1.20 (1.04, 1.38)	0.0102	
>=30 mL	32/ 51 (62.7)	18/ 39 (46.2)	1.37 (0.92, 2.03)	0.1196	
Baseline Volume of Hematoma 2					0.7712
<0.5 mL	5/ 7 (71.4)	8/ 11 (72.7)	1.15 (0.73, 1.81)	0.5446	
>=0.5 mL	166/ 234 (70.9)	127/ 221 (57.5)	1.23 (1.08, 1.42)	0.0025	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	151/ 215 (70.2)	125/ 218 (57.3)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	0/ 1 (0.0)			
Intracranial - subdural	10/ 13 (76.9)	4/ 5 (80.0)			
Intracranial - subarachnoid	9/ 10 (90.0)	6/ 8 (75.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.8234
<8 hours	64/ 101 (63.4)	53/ 103 (51.5)	1.21 (0.96, 1.53)	0.1100	
>=8 hours	104/ 133 (78.2)	82/ 130 (63.1)	1.25 (1.07, 1.46)	0.0061	
Intended Usual Care Agent					0.1899
PCC	103/ 160 (64.4)	80/ 156 (51.3)	1.26 (1.04, 1.52)	0.0161	
Other	15/ 18 (83.3)	10/ 11 (90.9)	0.92 (0.69, 1.23)	0.5720	
Unknown	53/ 63 (84.1)	45/ 66 (68.2)	1.21 (1.00, 1.46)	0.0504	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.2
Effective Hemostasis: No neurologic deterioration (NIHSS >= 7) (Assessed at 12 Hours Post-Randomization)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	211/241 (87.6)	201/233 (86.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.01 (0.95, 1.09)	
p-value	0.6934	
Odds Ratio (95% CI)	1.11 (0.65, 1.90)	
p-value	0.6933	
Risk Difference (95% CI)	1.22 (-4.84, 7.27)	
p-value	0.6933	
p-value of CMH-Test	0.6938	
p-value of Breslow-Day Test	0.9299	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.2.1
Effective Hemostasis: No neurologic deterioration (NIHSS >= 7) (Assessed at 12 Hours Post-Randomization) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.8793
<65 years	12/ 13 (92.3)	15/ 16 (93.8)	0.97 (0.79, 1.19)	0.7456	
65 - 74 years	38/ 45 (84.4)	41/ 51 (80.4)	1.04 (0.86, 1.25)	0.6939	
>=75 years	161/ 183 (88.0)	145/ 166 (87.3)	1.01 (0.93, 1.09)	0.8187	
Sex					0.2602
Male	113/ 130 (86.9)	97/ 118 (82.2)	1.06 (0.95, 1.18)	0.3107	
Female	98/ 111 (88.3)	104/ 115 (90.4)	0.98 (0.89, 1.07)	0.5879	
Race					0.4023
White	188/ 217 (86.6)	184/ 213 (86.4)	1.00 (0.93, 1.08)	0.9517	
Other	14/ 15 (93.3)	13/ 16 (81.3)	1.12 (0.88, 1.43)	0.3713	
Geographic Region 1					0.7394
North America	25/ 29 (86.2)	22/ 27 (81.5)	1.05 (0.85, 1.30)	0.6536	
Europe	186/ 212 (87.7)	179/ 206 (86.9)	1.01 (0.94, 1.09)	0.7795	
Prior FXa Inhibitor					0.4373
Apixaban	144/ 162 (88.9)	136/ 158 (86.1)	1.03 (0.95, 1.12)	0.4391	
Rivaroxaban	67/ 79 (84.8)	65/ 75 (86.7)	0.97 (0.86, 1.11)	0.6719	
Indication for prior FXa Inhibitor 1					0.6195
Atrial Fibrillation/Flutter	183/ 208 (88.0)	166/ 194 (85.6)	1.03 (0.95, 1.11)	0.5109	
Venous Thromboembolism	18/ 20 (90.0)	28/ 31 (90.3)	0.97 (0.80, 1.17)	0.7417	
Other	10/ 13 (76.9)	7/ 8 (87.5)	0.87 (0.59, 1.27)	0.4635	
Indication for prior FXa Inhibitor 2					0.3817
Atrial Fibrillation/Flutter	183/ 208 (88.0)	166/ 194 (85.6)	1.03 (0.95, 1.11)	0.5109	
Other	28/ 33 (84.8)	35/ 39 (89.7)	0.94 (0.79, 1.13)	0.5018	
Baseline Anti-FXa Activity 1					0.0509
<30 ng/mL	12/ 15 (80.0)	11/ 11 (100.0)	0.80 (0.62, 1.03)	0.0841	
>=30 ng/mL	187/ 211 (88.6)	172/ 202 (85.1)	1.04 (0.97, 1.12)	0.2971	
Baseline Anti-FXa Activity 2					0.8149
<75 ng/mL	59/ 67 (88.1)	44/ 52 (84.6)	1.04 (0.90, 1.20)	0.5928	
>=75 ng/mL	140/ 159 (88.1)	139/ 161 (86.3)	1.02 (0.94, 1.11)	0.6424	
ICH Score at baseline					0.2714
< 3	180/ 203 (88.7)	181/ 204 (88.7)	1.00 (0.93, 1.07)	0.9905	
>= 3	31/ 38 (81.6)	20/ 29 (69.0)	1.18 (0.88, 1.58)	0.2593	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.2.1
Effective Hemostasis: No neurologic deterioration (NIHSS >= 7) (Assessed at 12 Hours Post-Randomization) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.4801
<30 mL	172/ 190 (90.5)	174/ 193 (90.2)	1.00 (0.94, 1.07)	0.9327	
>=30 mL	39/ 51 (76.5)	27/ 39 (69.2)	1.10 (0.85, 1.43)	0.4537	
Baseline Volume of Hematoma 2					NE
<0.5 mL	7/ 7 (100.0)	11/ 11 (100.0)	NE		
>=0.5 mL	204/ 234 (87.2)	190/ 221 (86.0)	1.01 (0.94, 1.09)	0.7042	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	186/ 215 (86.5)	187/ 218 (85.8)			
Intracranial - intraventricular hemorrhage	2/ 2 (100.0)	1/ 1 (100.0)			
Intracranial - subdural	12/ 13 (92.3)	5/ 5 (100.0)			
Intracranial - subarachnoid	10/ 10 (100.0)	8/ 8 (100.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.7648
<8 hours	86/ 101 (85.1)	85/ 103 (82.5)	1.03 (0.91, 1.16)	0.6737	
>=8 hours	119/ 133 (89.5)	116/ 130 (89.2)	1.00 (0.92, 1.09)	0.9358	
Intended Usual Care Agent					0.5791
PCC	139/ 160 (86.9)	133/ 156 (85.3)	1.02 (0.93, 1.11)	0.6708	
Other	17/ 18 (94.4)	11/ 11 (100.0)	0.95 (0.85, 1.05)	0.3174	
Unknown	55/ 63 (87.3)	57/ 66 (86.4)	1.00 (0.88, 1.14)	0.9877	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.3
Effective Hemostasis: No administration of rescue therapy
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	235/241 (97.5)	218/233 (93.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.04 (1.00, 1.08)	
p-value	0.0403	
Odds Ratio (95% CI)	2.68 (1.02, 7.06)	
p-value	0.0454	
Risk Difference (95% CI)	3.91 (0.21, 7.62)	
p-value	0.0385	
p-value of CMH-Test	0.0384	
p-value of Breslow-Day Test	0.6078	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.3.1
Effective Hemostasis: No administration of rescue therapy - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.6940
<65 years	12/ 13 (92.3)	14/ 16 (87.5)	1.03 (0.81, 1.30)	0.8245	
65 - 74 years	44/ 45 (97.8)	46/ 51 (90.2)	1.08 (0.97, 1.19)	0.1473	
>=75 years	179/ 183 (97.8)	158/ 166 (95.2)	1.03 (0.99, 1.07)	0.1784	
Sex					0.4777
Male	128/ 130 (98.5)	110/ 118 (93.2)	1.06 (1.00, 1.11)	0.0456	
Female	107/ 111 (96.4)	108/ 115 (93.9)	1.03 (0.97, 1.09)	0.3871	
Race					0.7600
White	211/ 217 (97.2)	199/ 213 (93.4)	1.04 (1.00, 1.09)	0.0645	
Other	15/ 15 (100.0)	15/ 16 (93.8)	1.06 (0.95, 1.19)	0.3174	
Geographic Region 1					0.4961
North America	27/ 29 (93.1)	25/ 27 (92.6)	1.00 (0.87, 1.14)	0.9637	
Europe	208/ 212 (98.1)	193/ 206 (93.7)	1.05 (1.01, 1.09)	0.0227	
Prior FXa Inhibitor					0.5971
Apixaban	157/ 162 (96.9)	148/ 158 (93.7)	1.04 (0.99, 1.09)	0.1654	
Rivaroxaban	78/ 79 (98.7)	70/ 75 (93.3)	1.06 (0.99, 1.13)	0.0972	
Indication for prior FXa Inhibitor 1					0.9672
Atrial Fibrillation/Flutter	204/ 208 (98.1)	183/ 194 (94.3)	1.04 (1.00, 1.08)	0.0560	
Venous Thromboembolism	19/ 20 (95.0)	28/ 31 (90.3)	1.06 (0.91, 1.23)	0.4634	
Other	12/ 13 (92.3)	7/ 8 (87.5)	1.06 (0.74, 1.51)	0.7505	
Indication for prior FXa Inhibitor 2					0.9074
Atrial Fibrillation/Flutter	204/ 208 (98.1)	183/ 194 (94.3)	1.04 (1.00, 1.08)	0.0560	
Other	31/ 33 (93.9)	35/ 39 (89.7)	1.05 (0.92, 1.20)	0.4956	
Baseline Anti-FXa Activity 1					0.1038
<30 ng/mL	14/ 15 (93.3)	11/ 11 (100.0)	0.94 (0.82, 1.07)	0.3174	
>=30 ng/mL	206/ 211 (97.6)	188/ 202 (93.1)	1.05 (1.00, 1.10)	0.0296	
Baseline Anti-FXa Activity 2					0.7671
<75 ng/mL	64/ 67 (95.5)	47/ 52 (90.4)	1.06 (0.95, 1.17)	0.2902	
>=75 ng/mL	156/ 159 (98.1)	152/ 161 (94.4)	1.04 (1.00, 1.09)	0.0811	
ICH Score at baseline					0.5135
< 3	200/ 203 (98.5)	194/ 204 (95.1)	1.04 (1.00, 1.07)	0.0494	
>= 3	35/ 38 (92.1)	24/ 29 (82.8)	1.10 (0.92, 1.33)	0.3004	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.3.1
Effective Hemostasis: No administration of rescue therapy - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.2982
<30 mL	186/ 190 (97.9)	184/ 193 (95.3)	1.03 (0.99, 1.07)	0.1699	
>=30 mL	49/ 51 (96.1)	34/ 39 (87.2)	1.10 (0.97, 1.26)	0.1407	
Baseline Volume of Hematoma 2					0.4343
<0.5 mL	7/ 7 (100.0)	10/ 11 (90.9)	1.18 (0.85, 1.62)	0.3179	
>=0.5 mL	228/ 234 (97.4)	208/ 221 (94.1)	1.04 (1.00, 1.08)	0.0803	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	209/ 215 (97.2)	204/ 218 (93.6)			
Intracranial - intraventricular hemorrhage	2/ 2 (100.0)	1/ 1 (100.0)			
Intracranial - subdural	13/ 13 (100.0)	5/ 5 (100.0)			
Intracranial - subarachnoid	10/ 10 (100.0)	8/ 8 (100.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.2737
<8 hours	97/ 101 (96.0)	92/ 103 (89.3)	1.07 (0.99, 1.16)	0.0704	
>=8 hours	132/ 133 (99.2)	126/ 130 (96.9)	1.02 (0.99, 1.06)	0.1623	
Intended Usual Care Agent					0.1159
PCC	156/ 160 (97.5)	143/ 156 (91.7)	1.06 (1.01, 1.12)	0.0233	
Other	17/ 18 (94.4)	11/ 11 (100.0)	0.95 (0.85, 1.05)	0.3174	
Unknown	62/ 63 (98.4)	64/ 66 (97.0)	1.01 (0.96, 1.06)	0.6975	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.2.4
Effective Hemostasis: No increase in hematoma volume >20% (Assessed at 12 Hours Post-Randomization)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	151/241 (62.7)	115/233 (49.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.27 (1.08, 1.49)	
p-value	0.0041	
Odds Ratio (95% CI)	1.73 (1.19, 2.51)	
p-value	0.0037	
Risk Difference (95% CI)	13.11 (4.35, 21.88)	
p-value	0.0034	
p-value of CMH-Test	0.0037	
p-value of Breslow-Day Test	0.5080	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.3
Proportion of Participants With Effective Hemostasis: Worst Case Scenario
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	151/241 (62.7)	124/233 (53.2)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.17 (1.01, 1.37)	
p-value	0.0403	
Odds Ratio (95% CI)	1.48 (1.02, 2.15)	
p-value	0.0393	
Risk Difference (95% CI)	9.22 (0.50, 17.95)	
p-value	0.0382	
p-value of CMH-Test	0.0392	
p-value of Breslow-Day Test	0.4364	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.3.1
Proportion of Participants With Effective Hemostasis: Worst Case Scenario - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.9505
<65 years	10/ 13 (76.9)	10/ 16 (62.5)	1.18 (0.74, 1.88)	0.4863	
65 - 74 years	25/ 45 (55.6)	22/ 51 (43.1)	1.25 (0.82, 1.90)	0.3040	
>=75 years	116/ 183 (63.4)	92/ 166 (55.4)	1.16 (0.97, 1.38)	0.0975	
Sex					0.2586
Male	80/ 130 (61.5)	56/ 118 (47.5)	1.29 (1.02, 1.62)	0.0311	
Female	71/ 111 (64.0)	68/ 115 (59.1)	1.08 (0.88, 1.32)	0.4577	
Race					0.5270
White	138/ 217 (63.6)	116/ 213 (54.5)	1.16 (1.00, 1.36)	0.0570	
Other	7/ 15 (46.7)	8/ 16 (50.0)	0.92 (0.44, 1.89)	0.8112	
Geographic Region 1					0.2306
North America	15/ 29 (51.7)	15/ 27 (55.6)	0.90 (0.57, 1.43)	0.6646	
Europe	136/ 212 (64.2)	109/ 206 (52.9)	1.22 (1.04, 1.43)	0.0166	
Prior FXa Inhibitor					0.4101
Apixaban	110/ 162 (67.9)	88/ 158 (55.7)	1.22 (1.03, 1.45)	0.0233	
Rivaroxaban	41/ 79 (51.9)	36/ 75 (48.0)	1.05 (0.77, 1.44)	0.7470	
Indication for prior FXa Inhibitor 1					0.5195
Atrial Fibrillation/Flutter	132/ 208 (63.5)	102/ 194 (52.6)	1.20 (1.01, 1.41)	0.0338	
Venous Thromboembolism	11/ 20 (55.0)	19/ 31 (61.3)	0.94 (0.58, 1.51)	0.7933	
Other	8/ 13 (61.5)	3/ 8 (37.5)	1.64 (0.60, 4.49)	0.3389	
Indication for prior FXa Inhibitor 2					0.5154
Atrial Fibrillation/Flutter	132/ 208 (63.5)	102/ 194 (52.6)	1.20 (1.01, 1.41)	0.0338	
Other	19/ 33 (57.6)	22/ 39 (56.4)	1.04 (0.70, 1.54)	0.8591	
Baseline Anti-FXa Activity 1					0.1003
<30 ng/mL	8/ 15 (53.3)	8/ 11 (72.7)	0.73 (0.39, 1.38)	0.3389	
>=30 ng/mL	133/ 211 (63.0)	100/ 202 (49.5)	1.27 (1.07, 1.51)	0.0056	
Baseline Anti-FXa Activity 2					0.9523
<75 ng/mL	46/ 67 (68.7)	29/ 52 (55.8)	1.23 (0.92, 1.64)	0.1555	
>=75 ng/mL	95/ 159 (59.7)	79/ 161 (49.1)	1.22 (1.00, 1.49)	0.0521	
ICH Score at baseline					0.3773
< 3	129/ 203 (63.5)	113/ 204 (55.4)	1.15 (0.98, 1.35)	0.0885	
>= 3	22/ 38 (57.9)	11/ 29 (37.9)	1.48 (0.86, 2.57)	0.1572	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.3.1
Proportion of Participants With Effective Hemostasis: Worst Case Scenario - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.5779
<30 mL	128/ 190 (67.4)	111/ 193 (57.5)	1.17 (1.00, 1.36)	0.0508	
>=30 mL	23/ 51 (45.1)	13/ 39 (33.3)	1.36 (0.80, 2.32)	0.2519	
Baseline Volume of Hematoma 2					0.8942
<0.5 mL	5/ 7 (71.4)	8/ 11 (72.7)	1.15 (0.73, 1.81)	0.5446	
>=0.5 mL	146/ 234 (62.4)	116/ 221 (52.5)	1.19 (1.02, 1.39)	0.0308	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	132/ 215 (61.4)	114/ 218 (52.3)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	0/ 1 (0.0)			
Intracranial - subdural	9/ 13 (69.2)	4/ 5 (80.0)			
Intracranial - subarachnoid	9/ 10 (90.0)	6/ 8 (75.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.3112
<8 hours	52/ 101 (51.5)	49/ 103 (47.6)	1.06 (0.81, 1.40)	0.6574	
>=8 hours	96/ 133 (72.2)	75/ 130 (57.7)	1.26 (1.05, 1.51)	0.0122	
Intended Usual Care Agent					0.1858
PCC	88/ 160 (55.0)	73/ 156 (46.8)	1.18 (0.95, 1.46)	0.1363	
Other	14/ 18 (77.8)	10/ 11 (90.9)	0.86 (0.63, 1.18)	0.3566	
Unknown	49/ 63 (77.8)	41/ 66 (62.1)	1.21 (0.97, 1.51)	0.0850	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.4
Proportion of Participants With Rescue therapies used between 3 and 12 hours post-randomization
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	6/241 (2.5)	15/233 (6.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.39 (0.15, 0.99)	
p-value	0.0464	
Odds Ratio (95% CI)	0.37 (0.14, 0.98)	
p-value	0.0454	
Risk Difference (95% CI)	-3.91 (-7.62, -0.21)	
p-value	0.0385	
p-value of CMH-Test	0.0384	
p-value of Breslow-Day Test	0.6078	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.4.1
Proportion of Participants With Rescue therapies used between 3 and 12 hours post-randomization - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.7699
<65 years	1/ 13 (7.7)	2/ 16 (12.5)	0.79 (0.09, 7.13)	0.8303	
65 - 74 years	1/ 45 (2.2)	5/ 51 (9.8)	0.26 (0.03, 1.97)	0.1927	
>=75 years	4/ 183 (2.2)	8/ 166 (4.8)	0.45 (0.14, 1.46)	0.1820	
Sex					0.3361
Male	2/ 130 (1.5)	8/ 118 (6.8)	0.23 (0.05, 1.05)	0.0580	
Female	4/ 111 (3.6)	7/ 115 (6.1)	0.60 (0.18, 1.97)	0.3953	
Race					0.9915
White	6/ 217 (2.8)	14/ 213 (6.6)	0.42 (0.17, 1.08)	0.0718	
Other	0/ 15 (0.0)	1/ 16 (6.3)	0.42 (0.02, 8.91)	0.5753	
Geographic Region 1					0.2923
North America	2/ 29 (6.9)	2/ 27 (7.4)	1.05 (0.13, 8.33)	0.9665	
Europe	4/ 212 (1.9)	13/ 206 (6.3)	0.30 (0.10, 0.89)	0.0308	
Prior FXa Inhibitor					0.4437
Apixaban	5/ 162 (3.1)	10/ 158 (6.3)	0.48 (0.17, 1.37)	0.1720	
Rivaroxaban	1/ 79 (1.3)	5/ 75 (6.7)	0.20 (0.02, 1.53)	0.1205	
Indication for prior FXa Inhibitor 1					0.9057
Atrial Fibrillation/Flutter	4/ 208 (1.9)	11/ 194 (5.7)	0.35 (0.11, 1.07)	0.0651	
Venous Thromboembolism	1/ 20 (5.0)	3/ 31 (9.7)	0.47 (0.05, 4.68)	0.5166	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.63 (0.05, 7.90)	0.7165	
Indication for prior FXa Inhibitor 2					0.6293
Atrial Fibrillation/Flutter	4/ 208 (1.9)	11/ 194 (5.7)	0.35 (0.11, 1.07)	0.0651	
Other	2/ 33 (6.1)	4/ 39 (10.3)	0.57 (0.10, 3.20)	0.5266	
Baseline Anti-FXa Activity 1					0.2608
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.18 (0.10, 46.92)	0.6182	
>=30 ng/mL	5/ 211 (2.4)	14/ 202 (6.9)	0.34 (0.13, 0.93)	0.0359	
Baseline Anti-FXa Activity 2					0.7377
<75 ng/mL	3/ 67 (4.5)	5/ 52 (9.6)	0.47 (0.12, 1.85)	0.2780	
>=75 ng/mL	3/ 159 (1.9)	9/ 161 (5.6)	0.34 (0.09, 1.22)	0.0978	
ICH Score at baseline					0.6163
< 3	3/ 203 (1.5)	10/ 204 (4.9)	0.30 (0.08, 1.08)	0.0645	
>= 3	3/ 38 (7.9)	5/ 29 (17.2)	0.48 (0.12, 1.88)	0.2939	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.1.4.1
Proportion of Participants With Rescue therapies used between 3 and 12 hours post-randomization - Subgroup analysis
Intent-To-Treat Set

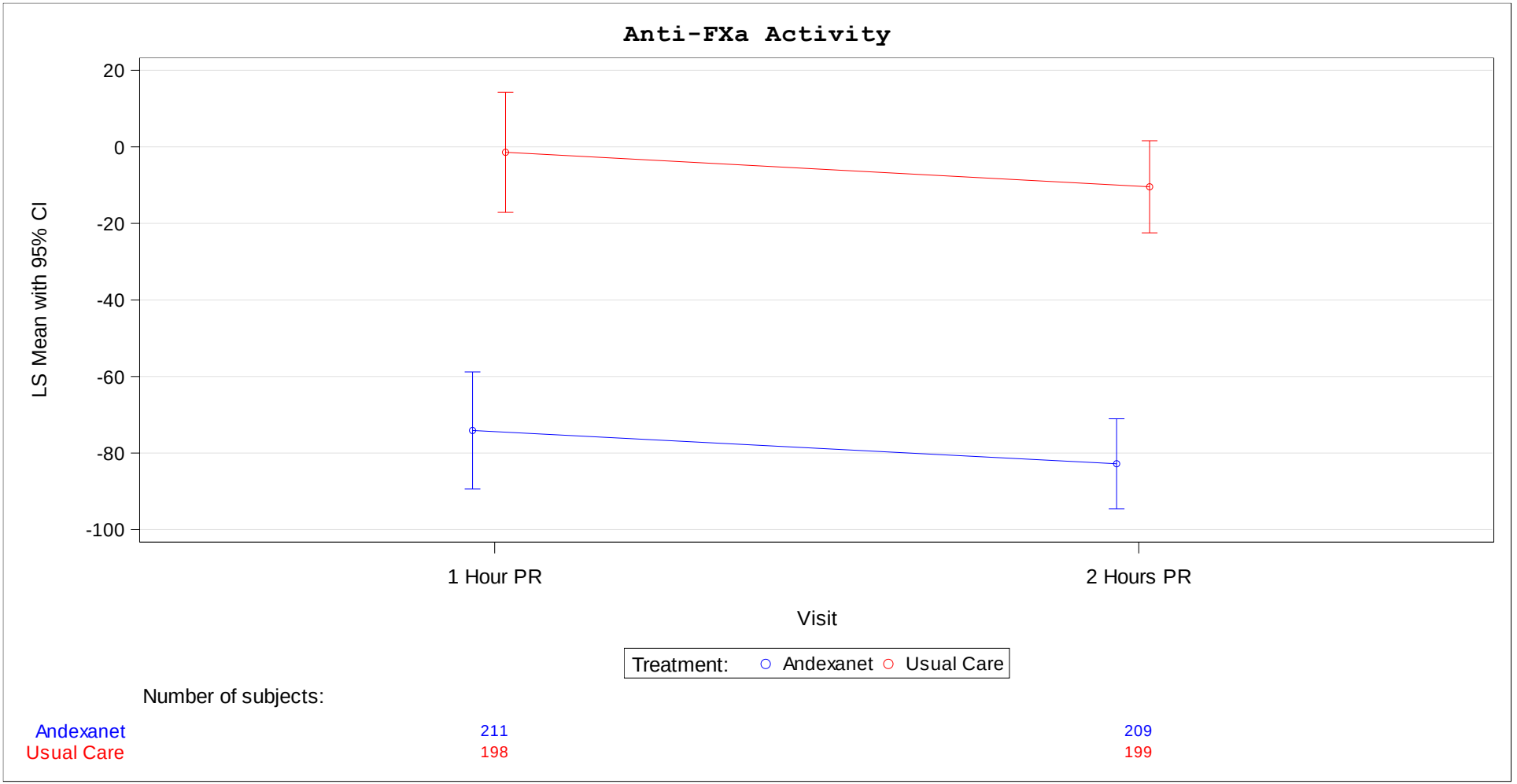
Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.6735
<30 mL	4/ 190 (2.1)	9/ 193 (4.7)	0.45 (0.14, 1.45)	0.1822	
>=30 mL	2/ 51 (3.9)	5/ 39 (12.8)	0.30 (0.06, 1.44)	0.1323	
Baseline Volume of Hematoma 2					0.7152
<0.5 mL	0/ 7 (0.0)	1/ 11 (9.1)	0.25 (0.01, 4.23)	0.3368	
>=0.5 mL	6/ 234 (2.6)	13/ 221 (5.9)	0.44 (0.17, 1.12)	0.0854	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	6/ 215 (2.8)	14/ 218 (6.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 13 (0.0)	0/ 5 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.7062
<8 hours	4/ 101 (4.0)	11/ 103 (10.7)	0.38 (0.12, 1.14)	0.0832	
>=8 hours	1/ 133 (0.8)	4/ 130 (3.1)	0.23 (0.03, 2.10)	0.1943	
Intended Usual Care Agent					0.5278
PCC	4/ 160 (2.5)	13/ 156 (8.3)	0.30 (0.10, 0.90)	0.0313	
Other	1/ 18 (5.6)	0/ 11 (0.0)	1.71 (0.08, 37.32)	0.7316	
Unknown	1/ 63 (1.6)	2/ 66 (3.0)	0.64 (0.06, 6.69)	0.7078	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.2.1
Summary of Mean Values and Percent Change from Baseline for Anti-FXa Activity (ng/mL) by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		% Change from Baseline		Value at Timepoint		% Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Anti-FXa Activity	Baseline	226	142.6 (102.77)			213	165.6 (124.75)		
	1 Hour Post Randomization	211	17.1 (20.18)	211	-75.2 (131.43)	198	133.8 (104.18)	198	-2.6 (76.45)
	2 Hours Post Randomization	209	9.7 (15.26)	209	-86.0 (55.40)	199	114.0 (91.04)	199	-12.3 (71.57)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation



CI: Confidence intervall, PR: Post Randomization

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.2.3
Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) at Nadir
Intent-To-Treat Set

Visit		Andexanet (N=241)	Usual Care (N=233)
Baseline	N	226	213
	Mean (SD)	142.55 (102.769)	165.61 (124.755)
Nadir	N	218	208
	Actual Value, Mean (SD)	9.58 (13.524)	102.75 (81.797)
	% Change From Baseline, Mean (SD)	-78.01 (139.063)	-22.86 (60.026)
	% Change From Baseline, LSMean (SE)	-80.47 (7.312)	-20.92 (7.494)
	Analysis Andexanet vs. Usual Care		
	Difference of LSMeans (95% CI)	-59.56 (-79.91, -39.20)	
	p-value	<.0001	
	Hedges'g (95% CI)	-0.55 (-0.74, -0.36)	
	p-value	<.0001	

Estimates are obtained from GLM for percent change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), baseline value as the covariates.
N describes number of patients included in the GLM, e.g. all patients with non-missing values at baseline and Nadir.
SD: Standard Deviation, SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Table 2.2.3.1
Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) at Nadir - Subgroup analysis
Intent-To-Treat Set

Subgroup	Andexanet (N=241)				Usual Care (N=233)				Difference of		Hedges'g (95% CI)	Interaction
	Baseline		% Change from BL		Baseline		% Change from BL					
Level	N	Mean (SD)	N	LSMean (SE)	N	Mean (SD)	N	LSMean (SE)	LSMeans (95% CI)	p-Value		p-Value
Age												0.2752
<65 years	12	128.2 (73.15)	10	-88.37 (8.85)	15	116.1 (74.66)	15	-24.56 (7.43)	-63.80 (-87.88, -39.73)	<.0001	-2.17 (-3.20, -1.13)	
65 - 74 years	39	146.9 (121.40)	38	-44.62 (33.93)	48	156.3 (108.28)	47	-41.79 (32.26)	-2.82 (-92.71, 87.06)	0.9503	-0.01 (-0.44, 0.41)	
>=75 years	175	142.6 (100.41)	170	-88.16 (4.83)	150	173.6 (132.61)	146	-15.76 (5.16)	-72.40 (-86.27, -58.54)	<.0001	-1.15 (-1.39, -0.91)	
Sex												0.7055
Male	120	138.5 (96.44)	117	-69.76 (13.38)	109	146.8 (117.97)	109	-14.79 (13.90)	-54.97 (-92.40, -17.54)	0.0042	-0.38 (-0.64, -0.11)	
Female	106	147.2 (109.78)	101	-91.65 (3.05)	104	185.3 (129.13)	99	-29.31 (3.08)	-62.33 (-70.84, -53.83)	<.0001	-2.03 (-2.37, -1.69)	
Race												0.4731
White	205	142.9 (102.67)	198	-79.36 (8.02)	194	167.2 (125.52)	189	-20.92 (8.22)	-58.44 (-80.80, -36.07)	<.0001	-0.52 (-0.72, -0.31)	
Other	12	154.2 (122.61)	12	-91.81 (6.58)	15	140.8 (128.05)	15	-23.06 (5.91)	-68.74 (-86.90, -50.59)	<.0001	-2.92 (-4.05, -1.78)	
Geographic Region 1												0.0406
North America	26	146.6 (120.09)	25	-88.60 (13.81)	22	149.3 (130.70)	22	14.83 (15.48)	-103.43 (-145.06, -61.80)	<.0001	-1.44 (-2.09, -0.79)	
Europe	200	142.0 (100.63)	193	-79.71 (8.06)	191	167.5 (124.27)	186	-24.52 (8.17)	-55.19 (-77.54, -32.84)	<.0001	-0.49 (-0.70, -0.29)	
Prior FXa Inhibitor												0.7258
Apixaban	152	124.3 (90.49)	148	-74.01 (10.38)	147	138.0 (95.93)	143	-13.26 (10.54)	-60.74 (-89.78, -31.71)	<.0001	-0.48 (-0.71, -0.25)	
Rivaroxaban	74	180.0 (116.21)	70	-93.96 (4.82)	66	227.1 (156.62)	65	-38.90 (5.12)	-55.06 (-68.37, -41.75)	<.0001	-1.34 (-1.72, -0.97)	
Indication for prior FXa Inhibitor 1												0.4815
Atrial Fibrillation/Flutter	195	139.1 (100.98)	188	-86.98 (4.35)	177	163.4 (121.42)	173	-17.59 (4.56)	-69.39 (-81.68, -57.10)	<.0001	-1.16 (-1.38, -0.93)	
Venous Thromboembolism	19	139.0 (116.65)	18	-3.31 (73.26)	29	172.2 (151.99)	28	-35.90 (54.00)	32.59 (-144.72, 209.90)	0.7126	0.11 (-0.48, 0.70)	
Other	12	203.6 (98.14)	12	-94.60 (5.68)	7	195.5 (90.84)	7	-29.61 (7.41)	-64.98 (-84.78, -45.19)	<.0001	-3.16 (-4.62, -1.70)	
Indication for prior FXa Inhibitor 2												0.2578
Atrial Fibrillation/Flutter	195	139.1 (100.98)	188	-86.98 (4.35)	177	163.4 (121.42)	173	-17.59 (4.56)	-69.39 (-81.68, -57.10)	<.0001	-1.16 (-1.38, -0.93)	
Other	31	164.0 (112.77)	30	-39.47 (45.38)	36	176.7 (141.36)	35	-37.42 (40.26)	-2.05 (-120.40, 116.31)	0.9725	-0.01 (-0.50, 0.48)	
Baseline Anti-FXa Activity 1												0.9260
<30 ng/mL	15	15.2 (9.89)	14	89.77 (109.43)	11	19.4 (6.73)	11	138.87 (125.69)	-49.10 (-396.43, 298.23)	0.7717	-0.12 (-0.91, 0.68)	
>=30 ng/mL	211	151.6 (100.34)	204	-92.68 (2.14)	202	173.6 (123.20)	197	-28.08 (2.18)	-64.61 (-70.56, -58.65)	<.0001	-2.11 (-2.35, -1.86)	
Baseline Anti-FXa Activity 2												0.7465
<75 ng/mL	67	46.7 (21.23)	65	-42.24 (23.28)	52	47.0 (18.12)	52	8.49 (26.04)	-50.72 (-119.35, 17.90)	0.1459	-0.27 (-0.63, 0.10)	
>=75 ng/mL	159	182.9 (96.53)	153	-93.91 (2.49)	161	203.9 (120.27)	156	-31.93 (2.47)	-61.97 (-68.79, -55.16)	<.0001	-2.00 (-2.28, -1.73)	
ICH Score at baseline												0.2522
< 3	188	139.1 (97.39)	182	-78.82 (8.57)	186	172.0 (129.07)	182	-21.85 (8.54)	-56.97 (-80.52, -33.42)	<.0001	-0.49 (-0.70, -0.28)	
>= 3	38	159.5 (126.21)	36	-88.91 (8.52)	27	121.7 (78.00)	26	-11.29 (10.34)	-77.62 (-104.61, -50.63)	<.0001	-1.48 (-2.05, -0.91)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM for percent change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), baseline value as the covariates.
N describes number of patients included in the GLM, e.g. all patients with non-missing values at baseline and Nadir.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Table 2.2.3.1
Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) at Nadir - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	% Change from BL N	% Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	% Change from BL N	% Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Baseline Volume of Hematoma 1												0.3335
<30 mL	176	143.4 (102.02)	171	-77.67 (9.05)	178	172.7 (130.57)	174	-21.32 (8.97)	-56.34 (-81.14, -31.54)	<.0001	-0.47 (-0.69, -0.26)	
>=30 mL	50	139.7 (106.37)	47	-89.94 (6.43)	34	123.5 (73.99)	33	-18.05 (7.71)	-71.89 (-91.77, -52.01)	<.0001	-1.61 (-2.13, -1.10)	
Baseline Volume of Hematoma 2												0.8173
<0.5 mL	6	106.6 (68.60)	6	-28.57 (97.45)	8	220.4 (86.23)	8	-3.41 (111.27)	-25.16 (-378.39, 328.06)	0.8770	-0.08 (-1.14, 0.98)	
>=0.5 mL	220	143.5 (103.47)	212	-82.78 (7.10)	204	162.6 (125.35)	199	-20.93 (7.32)	-61.85 (-81.69, -42.01)	<.0001	-0.60 (-0.80, -0.40)	
Index Bleeding Location 1												
Intracranial - intracerebral hemorrhage	205	140.7 (104.50)	197		198	166.2 (126.46)	195					
Intracranial - intraventricular hemorrhage	2	156.0 (103.03)	2		1	54.9 (-)	1					
Intracranial - subdural	10	187.5 (92.20)	10		5	179.9 (99.60)	4					
Intracranial - subarachnoid	9	132.5 (69.98)	9		8	134.8 (89.75)	7					
Time to Randomization since the last FXa Inhibitor Dose												0.3401
<8 hours	96	162.4 (116.02)	93	-86.72 (7.02)	96	202.3 (145.92)	95	-17.58 (7.05)	-69.13 (-88.23, -50.03)	<.0001	-1.01 (-1.31, -0.71)	
>=8 hours	124	125.2 (88.88)	119	-74.35 (12.14)	117	135.5 (94.78)	113	-24.12 (12.41)	-50.23 (-84.29, -16.17)	0.0040	-0.38 (-0.64, -0.12)	
Intended Usual Care Agent												0.1645
PCC	154	141.6 (106.85)	146	-75.46 (10.42)	149	165.9 (129.00)	148	-23.18 (10.30)	-52.28 (-80.64, -23.91)	0.0003	-0.42 (-0.65, -0.18)	
Other	18	126.6 (96.58)	18	-82.18 (7.87)	10	184.8 (147.49)	10	-27.35 (9.70)	-54.83 (-80.60, -29.06)	0.0002	-1.64 (-2.54, -0.74)	
Unknown	54	150.6 (93.44)	54	-95.56 (7.76)	54	161.3 (109.57)	50	-13.95 (8.14)	-81.61 (-103.99, -59.23)	<.0001	-1.41 (-1.85, -0.98)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM for percent change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), baseline value as the covariates.
N describes number of patients included in the GLM, e.g. all patients with non-missing values at baseline and Nadir.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Table 2.2.4
Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) at Nadir by Ranked ANCOVA
Intent-To-Treat Set

Visit		Andexanet (N=241)	Usual Care (N=233)
Nadir	N	226	213
	% Change From Baseline, LSMean (SE)	121.69 (4.669)	326.71 (4.804)
	Analysis Andexanet vs. Usual Care		
	Difference of LSMeans (95% CI)	-205.03 (-218.04, -192.01)	
	p-value	<.0001	
	Hedges'g (95% CI)	-2.92 (-3.19, -2.65)	
	p-value	<.0001	

Missing data are imputed using multiple imputation. Ranked ANCOVA is applied on ranked percent change from baseline at nadir, adjusting time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) and baseline anti-FXa activity.
N describes number of patients included in the model, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean.

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Table 2.2.5
MMRM Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
Anti-FXa Activity	1 Hour Post Randomization		-74.10 (7.78)		-1.42 (7.98)	-72.68 (-94.46, -50.89)	<.0001	-0.63 (-0.83, -0.44)
	2 Hours Post Randomization		-82.80 (5.97)		-10.44 (6.11)	-72.36 (-89.02, -55.69)	<.0001	-0.82 (-1.02, -0.62)
	Average Through Time	218	-78.45 (6.68)	208	-5.93 (6.85)	-72.52 (-91.18, -53.86)	<.0001	-0.73 (-0.93, -0.54)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.2.5.1
MMRM Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) % Change from BL N	Andexanet (N=241) % Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) % Change from BL N	Usual Care (N=233) % Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Anti-FXa Activity	Age												0.1806
	<65 years	12	128.2 (73.15)	10	-83.99 (18.12)	15	116.1 (74.66)	15	1.62 (15.14)	-85.60 (-134.68, -36.53)	0.0016	-1.42 (-2.33, -0.52)	
	65 - 74 years	39	146.9 (121.40)	38	-55.09 (20.15)	48	156.3 (108.28)	47	-22.43 (18.62)	-32.66 (-88.34, 23.03)	0.2389	-0.26 (-0.69, 0.17)	
	>=75 years	175	142.6 (100.41)	170	-85.48 (4.86)	150	173.6 (132.61)	146	-1.30 (5.20)	-84.18 (-98.16, -70.21)	<.0001	-1.33 (-1.57, -1.09)	
	Sex												0.5586
	Male	120	138.5 (96.44)	117	-67.17 (12.57)	109	146.8 (117.97)	109	-0.98 (13.05)	-66.19 (-101.46, -30.93)	0.0003	-0.48 (-0.75, -0.22)	
	Female	106	147.2 (109.78)	101	-89.54 (3.52)	104	185.3 (129.13)	99	-12.49 (3.57)	-77.05 (-86.92, -67.18)	<.0001	-2.17 (-2.52, -1.81)	
	Race												0.5718
	White	205	142.9 (102.67)	198	-77.67 (7.47)	194	167.2 (125.52)	189	-6.21 (7.66)	-71.46 (-92.35, -50.58)	<.0001	-0.68 (-0.88, -0.47)	
	Other	12	154.2 (122.61)	12	-84.51 (16.15)	15	140.8 (128.05)	15	0.69 (14.74)	-85.19 (-130.33, -40.06)	0.0007	-1.46 (-2.33, -0.59)	
	Geographic Region 1												0.0191
	North America	26	146.6 (120.09)	25	-84.15 (16.00)	22	149.3 (130.70)	22	43.72 (17.71)	-127.87 (-175.79, -79.96)	<.0001	-1.54 (-2.20, -0.88)	
	Europe	200	142.0 (100.63)	193	-77.96 (7.46)	191	167.5 (124.27)	186	-11.03 (7.58)	-66.93 (-87.69, -46.17)	<.0001	-0.65 (-0.85, -0.44)	
	Prior FXa Inhibitor												0.6202
	Apixaban	152	124.3 (90.49)	148	-71.35 (9.37)	147	138.0 (95.93)	143	3.19 (9.53)	-74.54 (-100.81, -48.27)	<.0001	-0.65 (-0.89, -0.42)	
	Rivaroxaban	74	180.0 (116.21)	70	-93.53 (5.34)	66	227.1 (156.62)	65	-26.56 (5.69)	-66.97 (-81.73, -52.20)	<.0001	-1.47 (-1.85, -1.09)	
	Indication for prior FXa Inhibitor 1												0.2630
	Atrial Fibrillation/Flutter	195	139.1 (100.98)	188	-83.99 (4.37)	177	163.4 (121.42)	173	-2.13 (4.59)	-81.86 (-94.24, -69.49)	<.0001	-1.36 (-1.59, -1.13)	
	Venous Thromboembolism	19	139.0 (116.65)	18	-26.98 (40.14)	29	172.2 (151.99)	28	-18.31 (31.57)	-8.67 (-115.51, 98.18)	0.8658	-0.05 (-0.64, 0.54)	
	Other	12	203.6 (98.14)	12	-90.43 (6.98)	7	195.5 (90.84)	7	-19.78 (9.11)	-70.65 (-94.97, -46.33)	<.0001	-2.80 (-4.16, -1.43)	
	Indication for prior FXa Inhibitor 2												0.1813
	Atrial Fibrillation/Flutter	195	139.1 (100.98)	188	-83.99 (4.37)	177	163.4 (121.42)	173	-2.13 (4.59)	-81.86 (-94.24, -69.49)	<.0001	-1.36 (-1.59, -1.13)	
	Other	31	164.0 (112.77)	30	-48.91 (28.50)	36	176.7 (141.36)	35	-19.29 (26.27)	-29.62 (-108.34, 49.10)	0.4484	-0.19 (-0.68, 0.30)	
	Baseline Anti-FXa Activity 1												0.7448
	<30 ng/mL	15	15.2 (9.89)	14	107.93 (71.85)	11	19.4 (6.73)	11	148.99 (81.52)	-41.06 (-260.24, 178.12)	0.7071	-0.15 (-0.94, 0.64)	
	>=30 ng/mL	211	151.6 (100.34)	204	-89.72 (2.48)	202	173.6 (123.20)	197	-13.32 (2.53)	-76.40 (-83.30, -69.51)	<.0001	-2.15 (-2.40, -1.90)	
	Baseline Anti-FXa Activity 2												0.9265
	<75 ng/mL	67	46.7 (21.23)	65	-43.43 (20.94)	52	47.0 (18.12)	52	30.50 (23.44)	-73.93 (-135.98, -11.89)	0.0200	-0.43 (-0.80, -0.07)	
	>=75 ng/mL	159	182.9 (96.53)	153	-91.04 (2.70)	161	203.9 (120.27)	156	-20.01 (2.68)	-71.03 (-78.42, -63.63)	<.0001	-2.12 (-2.40, -1.84)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.2.5.1
MMRM Analysis of Percent Change From Baseline in Anti-FXa Activity (ng/mL) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) % Change from BL N	Andexanet (N=241) % Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) % Change from BL N	Usual Care (N=233) % Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Anti-FXa Activity	ICH Score at baseline												0.1428
	< 3	188	139.1 (97.39)	182	-76.20 (7.72)	186	172.0 (129.07)	182	-7.87 (7.71)	-68.32 (-89.66, -46.99)	<.0001	-0.66 (-0.87, -0.44)	
	>= 3	38	159.5 (126.21)	36	-86.56 (9.44)	27	121.7 (78.00)	26	8.75 (11.37)	-95.31 (-125.09, -65.52)	<.0001	-1.65 (-2.23, -1.06)	
	Baseline Volume of Hematoma 1												0.2105
	<30 mL	176	143.4 (102.02)	171	-75.68 (8.18)	178	172.7 (130.57)	174	-7.14 (8.11)	-68.54 (-91.04, -46.04)	<.0001	-0.64 (-0.86, -0.42)	
	>=30 mL	50	139.7 (106.37)	47	-87.33 (7.09)	34	123.5 (73.99)	33	1.14 (8.57)	-88.47 (-110.51, -66.43)	<.0001	-1.79 (-2.32, -1.26)	
	Baseline Volume of Hematoma 2												0.7770
	<0.5 mL	6	106.6 (68.60)	6	-29.06 (107.23)	8	220.4 (86.23)	8	-4.39 (125.23)	-24.67 (-426.63, 377.28)	0.8940	-0.07 (-1.13, 0.99)	
	>=0.5 mL	220	143.5 (103.47)	212	-81.39 (6.00)	204	162.6 (125.35)	199	-5.55 (6.19)	-75.84 (-92.70, -58.99)	<.0001	-0.87 (-1.07, -0.66)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	205	140.7 (104.50)	197		198	166.2 (126.46)	195					
	Intracranial - intraventricular hemorrhage	2	156.0 (103.03)	2		1	54.9 (-)	1					
	Intracranial - subdural	10	187.5 (92.20)	10		5	179.9 (99.60)	4					
	Intracranial - subarachnoid	9	132.5 (69.98)	9		8	134.8 (89.75)	7					
	Time to Randomization since the last FXa Inhibitor Dose												0.2640
	<8 hours	96	162.4 (116.02)	93	-84.04 (6.67)	96	202.3 (145.92)	95	-0.26 (6.72)	-83.78 (-102.01, -65.54)	<.0001	-1.29 (-1.60, -0.97)	
	>=8 hours	124	125.2 (88.88)	119	-73.57 (10.41)	117	135.5 (94.78)	113	-9.32 (10.66)	-64.25 (-93.57, -34.93)	<.0001	-0.56 (-0.83, -0.30)	
	Intended Usual Care Agent												0.2666
	PCC	154	141.6 (106.85)	146	-74.57 (9.23)	149	165.9 (129.00)	148	-6.60 (9.13)	-67.97 (-93.27, -42.68)	<.0001	-0.61 (-0.84, -0.38)	
	Other	18	126.6 (96.58)	18	-80.91 (7.39)	10	184.8 (147.49)	10	-19.10 (9.02)	-61.81 (-85.92, -37.69)	<.0001	-1.97 (-2.93, -1.02)	
	Unknown	54	150.6 (93.44)	54	-91.06 (8.33)	54	161.3 (109.57)	50	-2.89 (8.74)	-88.17 (-112.17, -64.17)	<.0001	-1.42 (-1.86, -0.99)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.1
Summary of Mean Values and Change from Baseline for Thrombin Generation Parameters by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Endogenous Thrombin Potential (nM x min)	Baseline	165	849.3 (455.52)			165	820.2 (610.34)		
	1 Hour Post Randomization	143	1621.5 (426.00)	143	779.3 (597.13)	110	1004.3 (661.61)	110	130.2 (877.38)
	12 Hours Post Randomization	143	1206.9 (303.28)	143	355.3 (443.09)	130	1488.3 (615.51)	130	672.2 (830.50)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.1
Summary of Mean Values and Change from Baseline for Thrombin Generation Parameters by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
ETP Lag Time (minutes)	Baseline	188	6.5 (3.03)			181	6.8 (3.02)		
	1 Hour Post Randomization	167	2.9 (0.95)	167	-3.7 (2.84)	140	7.0 (3.27)	140	0.3 (2.73)
	12 Hours Post Randomization	164	3.8 (1.25)	164	-2.6 (2.44)	151	5.7 (2.47)	151	-1.2 (2.97)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation

Table 2.3.1
Summary of Mean Values and Change from Baseline for Thrombin Generation Parameters by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
ETP Peak Height (nM)	Baseline	188	70.6 (65.34)			181	67.1 (62.84)		
	1 Hour Post Randomization	167	279.4 (87.27)	167	209.3 (98.65)	140	76.0 (80.42)	140	6.2 (72.00)
	12 Hours Post Randomization	164	152.6 (72.11)	164	83.4 (68.18)	151	140.8 (183.96)	151	75.0 (183.65)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.1
Summary of Mean Values and Change from Baseline for Thrombin Generation Parameters by Visit
Intent-To-Treat Set

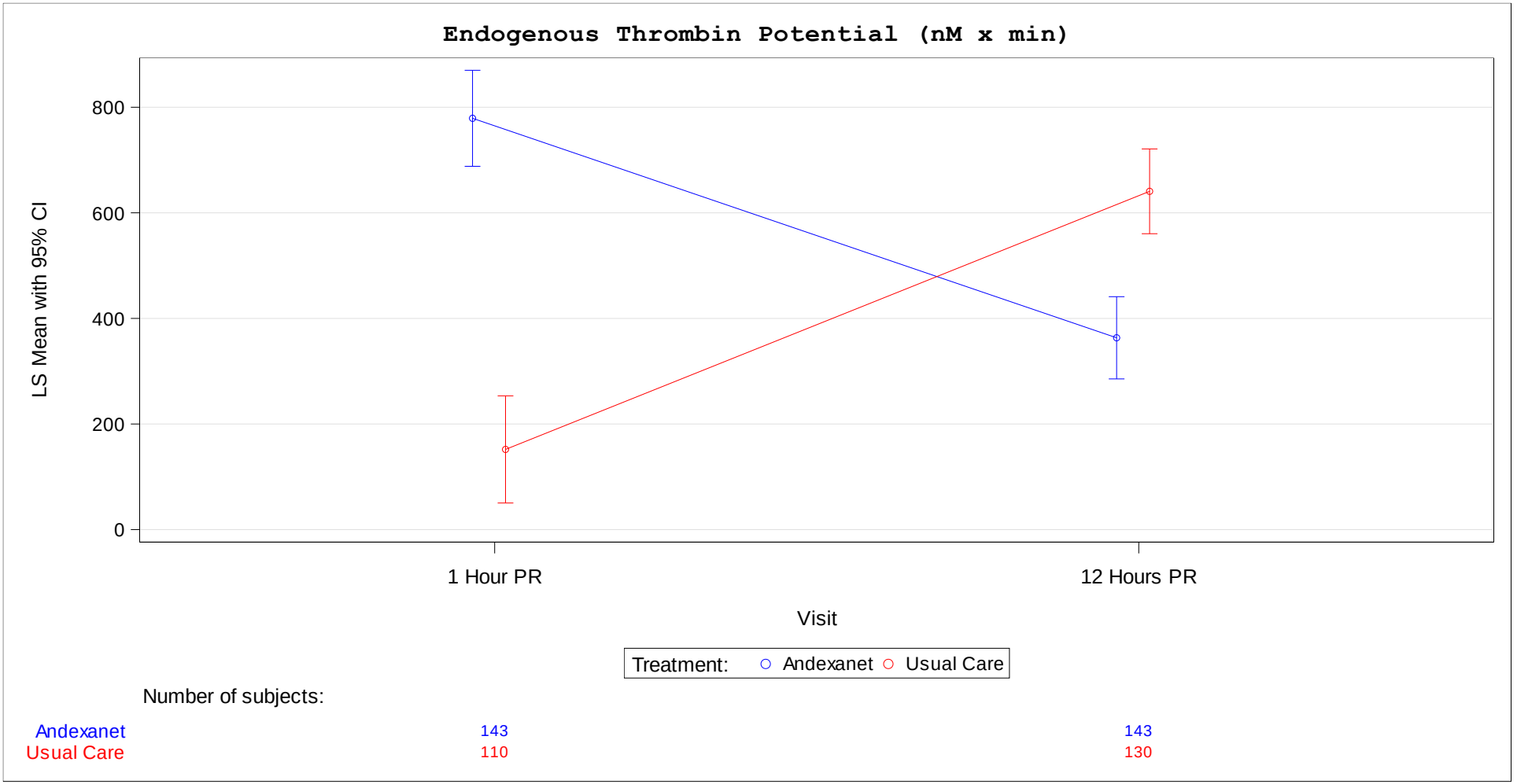
		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
ETP Time to Peak (minutes)	Baseline	188	12.9 (6.52)			181	12.7 (6.04)		
	1 Hour Post Randomization	167	5.9 (2.95)	167	-6.9 (5.99)	140	14.9 (7.63)	140	2.3 (7.26)
	12 Hours Post Randomization	164	8.3 (3.82)	164	-4.6 (5.05)	151	11.3 (4.30)	151	-1.4 (5.56)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation

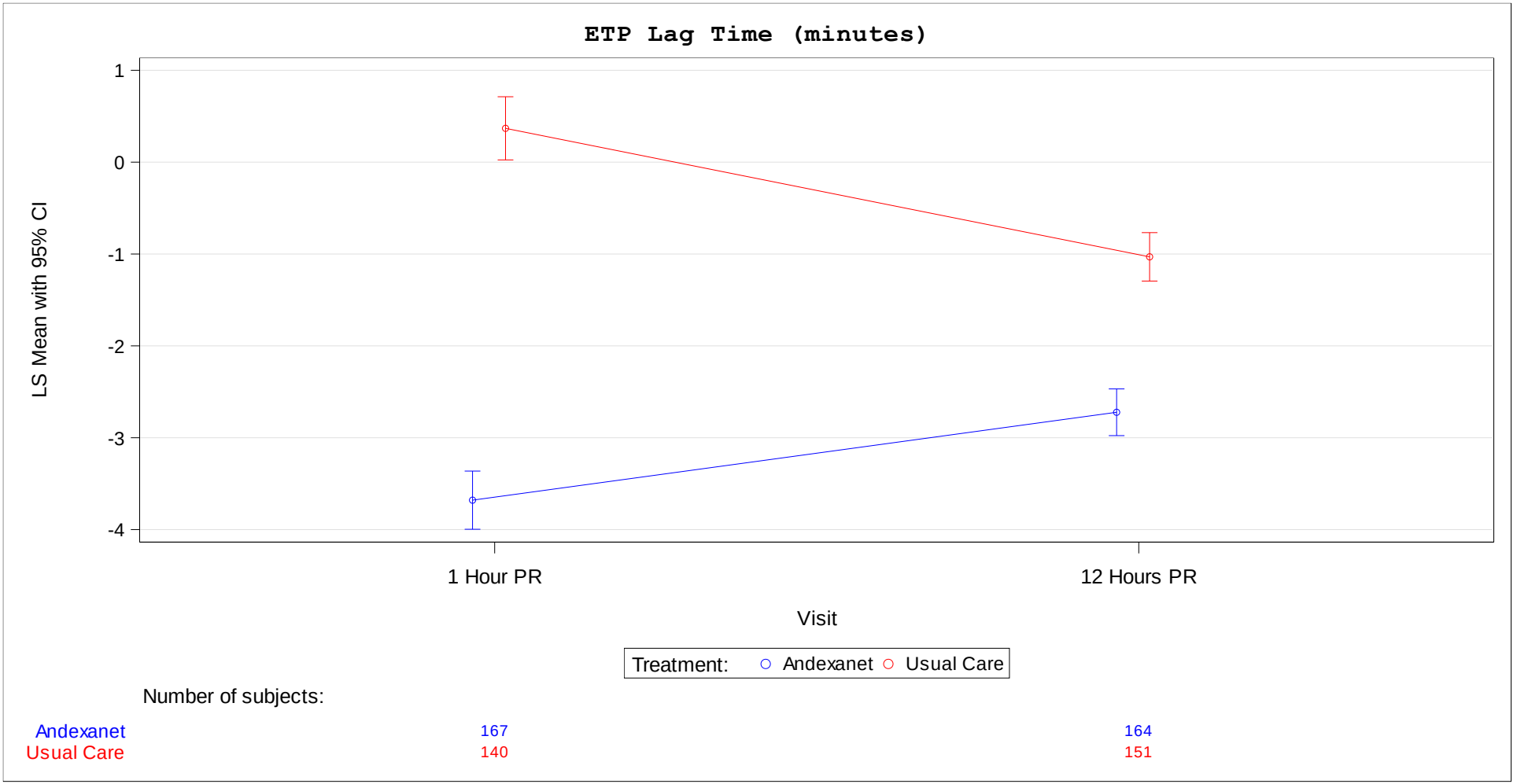
AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.1
Summary of Mean Values and Change from Baseline for Thrombin Generation Parameters by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
ETP Velocity Index (nM/min)	Baseline	188	19.7 (30.05)			181	19.0 (29.49)		
	1 Hour Post Randomization	167	116.7 (50.67)	167	96.9 (52.50)	140	19.2 (31.84)	140	-1.1 (32.95)
	12 Hours Post Randomization	164	50.7 (37.19)	164	31.9 (37.19)	151	46.8 (177.38)	151	28.9 (176.80)

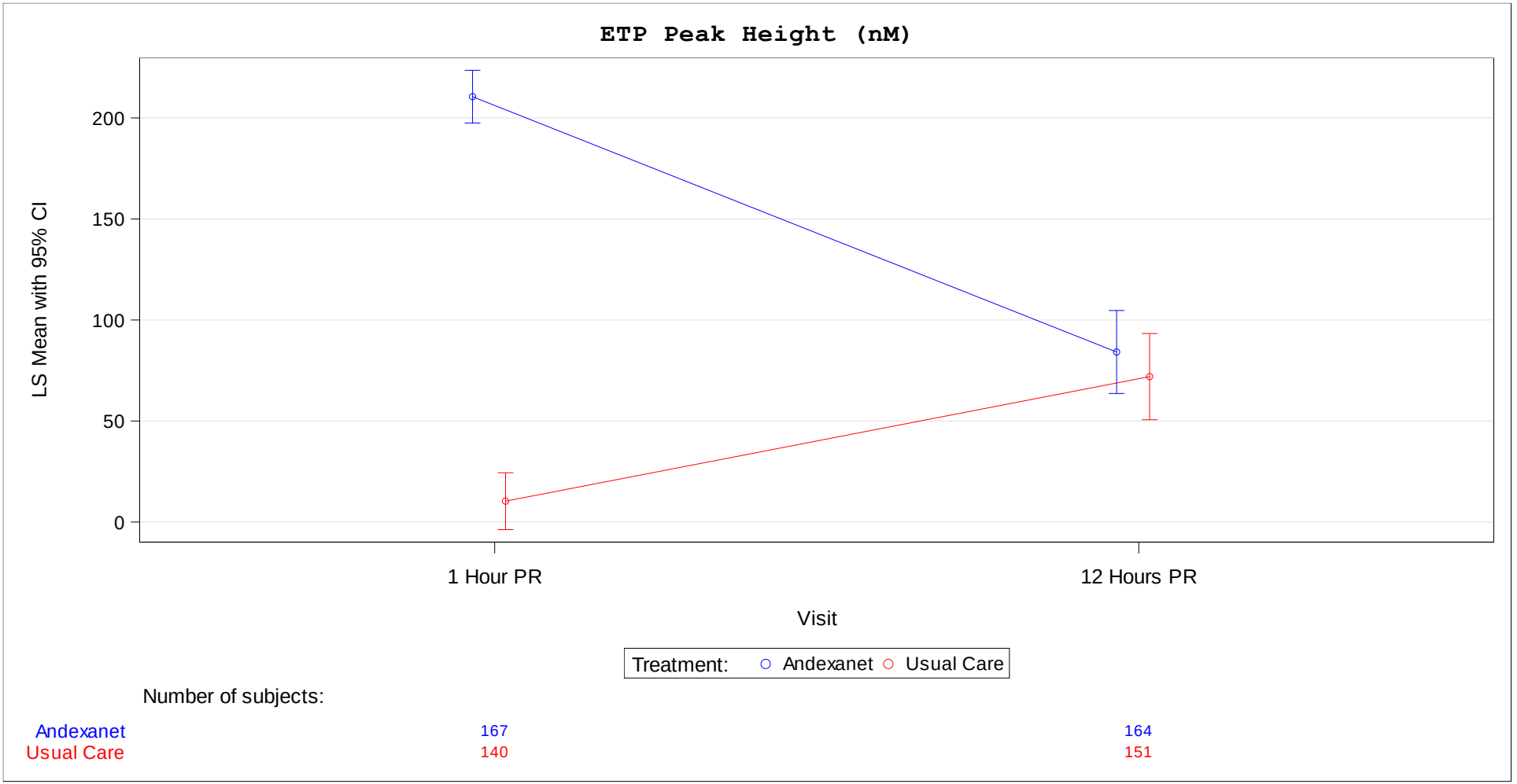
N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation



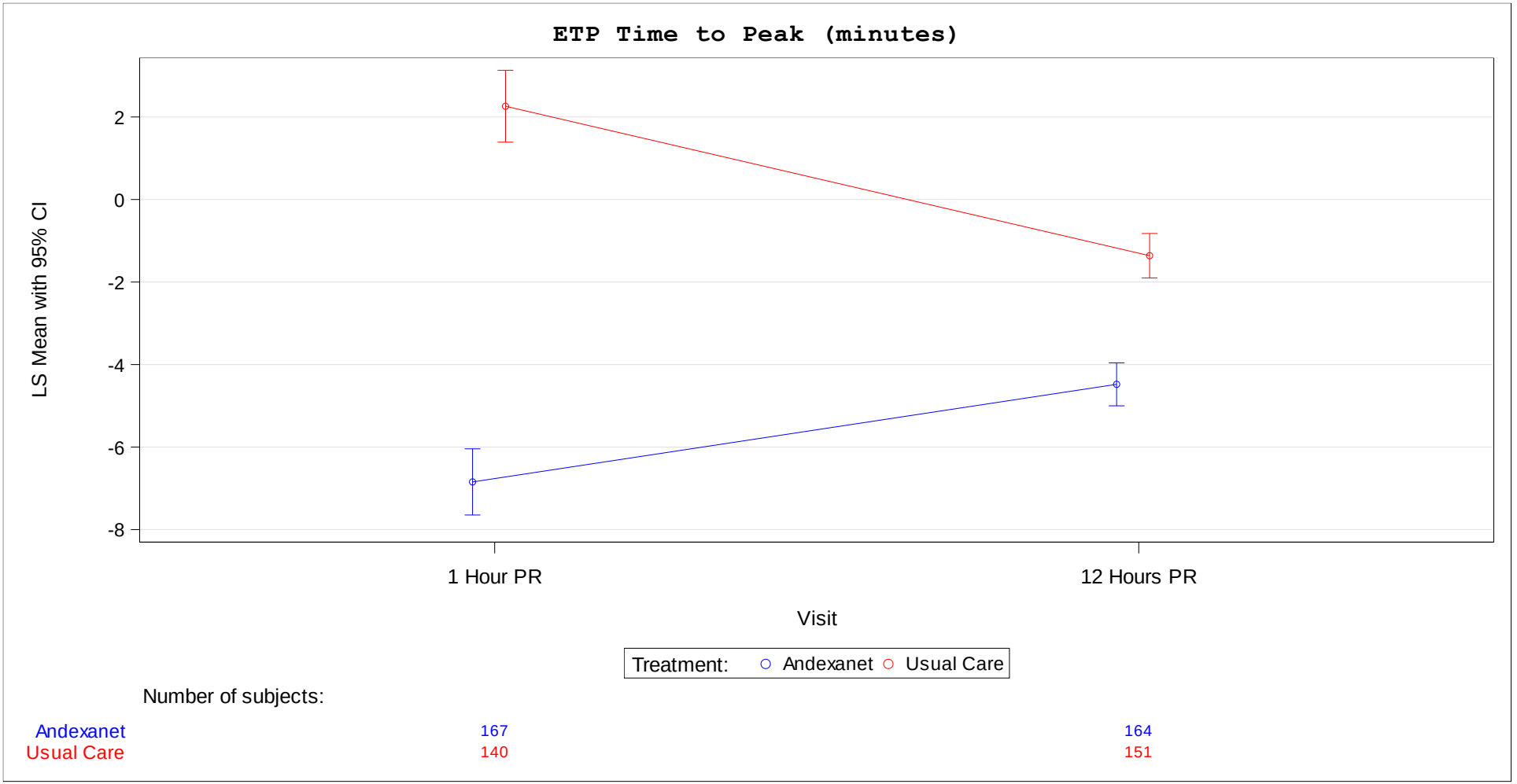
CI: Confidence intervall, PR: Post Randomization



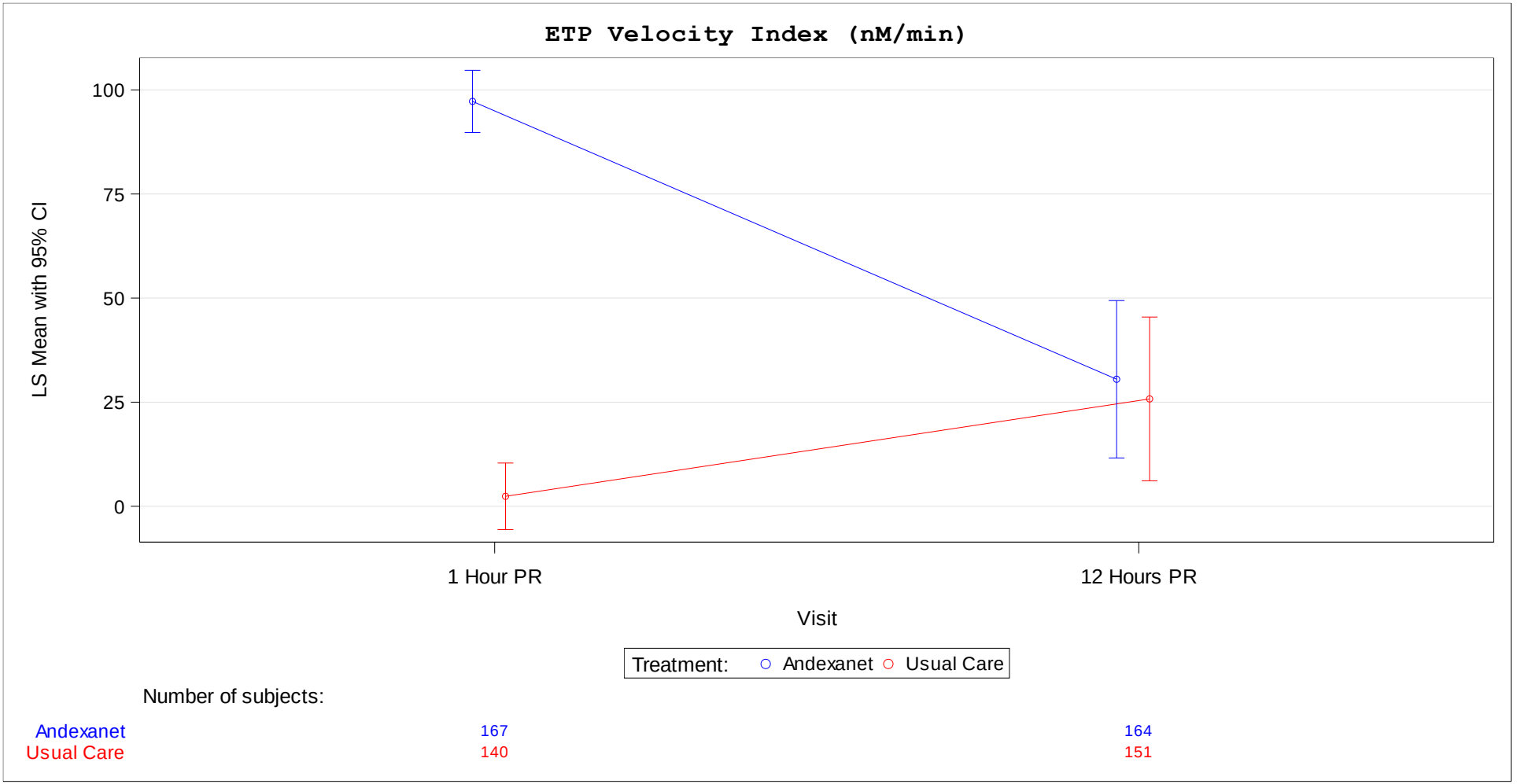
CI: Confidence intervall, PR: Post Randomization



CI: Confidence intervall, PR: Post Randomization



CI: Confidence intervall, PR: Post Randomization



CI: Confidence intervall, PR: Post Randomization

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
Endogenous Thrombin Potential (nM x min)	1 Hour Post Randomization		779.02 (46.16)		151.87 (51.52)	627.15 (492.24, 762.07)	<.0001	1.05 (0.80, 1.29)
	12 Hours Post Randomization		363.29 (39.56)		640.71 (40.79)	-277.43 (-387.88, -166.97)	<.0001	-0.56 (-0.79, -0.33)
	Average Through Time	156	571.15 (35.96)	145	396.29 (38.03)	174.86 (73.45, 276.28)	0.0008	0.38 (0.16, 0.61)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.3.3
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
ETP Lag Time (minutes)	1 Hour Post Randomization		-3.68 (0.16)		0.37 (0.17)	-4.05 (-4.51, -3.58)	<.0001	-1.83 (-2.08, -1.58)
	12 Hours Post Randomization		-2.72 (0.13)		-1.03 (0.13)	-1.69 (-2.05, -1.33)	<.0001	-0.97 (-1.20, -0.75)
	Average Through Time	180	-3.20 (0.12)	167	-0.33 (0.12)	-2.87 (-3.20, -2.54)	<.0001	-1.80 (-2.05, -1.55)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.3.3
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241)		Usual Care (N=233)		Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
		N	LSMean (SE)	N	LSMean (SE)			
ETP Peak Height (nM)	1 Hour Post Randomization		210.53 (6.61)		10.32 (7.14)	200.20 (181.31, 219.10)	<.0001	2.21 (1.94, 2.48)
	12 Hours Post Randomization		84.16 (10.44)		71.97 (10.84)	12.19 (-17.24, 41.61)	0.4158	0.09 (-0.12, 0.30)
	Average Through Time	180	147.34 (7.22)	167	41.15 (7.54)	106.20 (85.89, 126.50)	<.0001	1.09 (0.86, 1.32)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.3.3
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
ETP Time to Peak (minutes)	1 Hour Post Randomization		-6.84 (0.41)		2.26 (0.44)	-9.11 (-10.28, -7.93)	<.0001	-1.63 (-1.87, -1.38)
	12 Hours Post Randomization		-4.48 (0.26)		-1.36 (0.27)	-3.12 (-3.86, -2.38)	<.0001	-0.88 (-1.10, -0.66)
	Average Through Time	180	-5.66 (0.27)	167	0.45 (0.29)	-6.11 (-6.89, -5.34)	<.0001	-1.64 (-1.89, -1.40)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.3.3
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241)		Usual Care (N=233)		Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
		N	LSMean (SE)	N	LSMean (SE)			
ETP Velocity Index (nM/min)	1 Hour Post Randomization		97.24 (3.75)		2.39 (4.03)	94.85 (84.09, 105.62)	<.0001	1.85 (1.60, 2.10)
	12 Hours Post Randomization		30.51 (9.61)		25.78 (10.00)	4.73 (-22.48, 31.93)	0.7328	0.04 (-0.17, 0.25)
	Average Through Time	180	63.87 (6.03)	167	14.08 (6.27)	49.79 (32.75, 66.83)	<.0001	0.61 (0.40, 0.83)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Endogenous Thrombin Potential (nM x min)	Age												0.8465
	<65 years	9	864.8 (261.78)	8	109.95 (219.80)	13	1430.8 (1858.83)	9	-21.59 (201.00)	131.54 (-502.88, 765.96)	0.6637	0.20 (-0.75, 1.16)	
	65 - 74 years	32	910.7 (391.91)	29	655.61 (77.37)	35	807.5 (318.51)	32	452.88 (77.44)	202.73 (-7.31, 412.76)	0.0582	0.47 (-0.04, 0.98)	
	>=75 years	124	832.3 (481.88)	119	576.75 (38.06)	117	756.1 (305.79)	104	442.01 (41.79)	134.74 (24.06, 245.42)	0.0173	0.32 (0.05, 0.58)	
	Sex												0.4871
	Male	87	858.0 (512.74)	83	541.44 (49.58)	90	848.4 (770.71)	80	349.29 (50.58)	192.15 (55.09, 329.20)	0.0063	0.42 (0.11, 0.73)	
	Female	78	839.6 (384.89)	73	606.13 (45.14)	75	786.4 (330.25)	65	481.36 (51.47)	124.77 (-9.59, 259.14)	0.0684	0.31 (-0.03, 0.65)	
	Race												0.2311
	White	146	828.1 (466.67)	138	564.19 (37.45)	148	796.0 (627.61)	134	390.99 (38.93)	173.20 (68.76, 277.65)	0.0012	0.39 (0.15, 0.63)	
	Other	10	1015.5 (336.17)	9	551.72 (189.62)	15	1069.3 (380.07)	10	701.86 (182.11)	-150.14 (-730.09, 429.81)	0.5816	-0.25 (-1.16, 0.65)	
	Geographic Region 1												0.8668
	North America	16	752.6 (238.14)	14	749.67 (157.99)	17	825.5 (343.11)	13	606.87 (180.63)	142.80 (-359.76, 645.35)	0.5559	0.22 (-0.53, 0.98)	
	Europe	149	859.7 (472.30)	142	557.84 (36.04)	148	819.6 (634.65)	132	374.28 (38.18)	183.56 (81.63, 285.49)	0.0005	0.42 (0.18, 0.66)	
	Prior FXa Inhibitor												0.0217
	Apixaban	112	892.4 (509.77)	105	552.58 (42.04)	110	796.0 (328.92)	100	469.59 (43.47)	82.99 (-35.62, 201.61)	0.1690	0.19 (-0.08, 0.47)	
	Rivaroxaban	53	758.1 (295.32)	51	581.43 (59.81)	55	868.5 (953.62)	45	255.68 (67.87)	325.75 (152.68, 498.82)	0.0003	0.73 (0.32, 1.15)	
	Indication for prior FXa Inhibitor 1												0.4953
	Atrial Fibrillation/Flutter	139	847.1 (452.84)	134	543.01 (35.50)	137	816.6 (651.01)	119	362.66 (38.70)	180.35 (78.51, 282.19)	0.0006	0.43 (0.18, 0.68)	
	Venous Thromboembolism	19	906.1 (531.73)	16	830.24 (141.24)	23	805.4 (368.17)	21	492.15 (118.00)	338.09 (-41.02, 717.19)	0.0782	0.60 (-0.07, 1.27)	
	Other	7	737.6 (286.61)	6	645.51 (250.02)	5	985.5 (286.71)	5	851.34 (362.73)	-205.83 (-1289.49, 877.83)	0.6703	-0.27 (-1.46, 0.93)	
	Indication for prior FXa Inhibitor 2												0.9275
	Atrial Fibrillation/Flutter	139	847.1 (452.84)	134	543.01 (35.50)	137	816.6 (651.01)	119	362.66 (38.70)	180.35 (78.51, 282.19)	0.0006	0.43 (0.18, 0.68)	
	Other	26	860.7 (478.64)	22	738.30 (121.49)	28	837.6 (357.16)	26	542.38 (108.99)	195.92 (-144.28, 536.11)	0.2437	0.34 (-0.23, 0.92)	
	Baseline Anti-FXa Activity 1												0.0518
	<30 ng/mL	12	1103.9 (371.13)	11	450.97 (114.51)	10	969.3 (427.01)	9	605.38 (136.30)	-154.41 (-522.08, 213.26)	0.3861	-0.38 (-1.27, 0.51)	
	>=30 ng/mL	147	820.7 (456.72)	140	587.74 (37.71)	152	809.7 (625.61)	134	389.59 (39.21)	198.14 (92.89, 303.39)	0.0003	0.44 (0.20, 0.68)	
	Baseline Anti-FXa Activity 2												0.1257
	<75 ng/mL	52	904.4 (323.58)	51	480.00 (64.98)	43	1092.8 (1037.47)	39	444.33 (74.81)	35.67 (-160.30, 231.64)	0.7184	0.08 (-0.34, 0.49)	
	>=75 ng/mL	107	811.7 (506.74)	100	598.62 (39.22)	119	720.9 (310.89)	104	390.22 (39.65)	208.40 (100.22, 316.58)	0.0002	0.52 (0.24, 0.80)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Endogenous Thrombin Potential (nM x min)	ICH Score at baseline												0.1029
	< 3	133	870.7 (463.12)	127	570.04 (41.15)	144	818.7 (648.81)	127	365.48 (41.85)	204.55 (90.80, 318.30)	0.0005	0.44 (0.19, 0.68)	
	>= 3	32	760.2 (417.49)	29	602.89 (66.30)	21	830.2 (211.48)	18	601.70 (89.25)	1.18 (-223.65, 226.02)	0.9915	0.00 (-0.58, 0.59)	
	Baseline Volume of Hematoma 1												0.6242
	<30 mL	124	845.2 (469.22)	118	551.51 (42.58)	136	831.2 (664.58)	119	377.83 (42.84)	173.68 (57.08, 290.28)	0.0037	0.37 (0.12, 0.63)	
	>=30 mL	41	861.7 (416.57)	38	627.32 (63.22)	29	768.4 (221.42)	26	511.25 (79.64)	116.08 (-87.52, 319.67)	0.2583	0.29 (-0.21, 0.79)	
	Baseline Volume of Hematoma 2												
	<0.5 mL	4	679.0 (293.94)	4		6	699.1 (556.51)	5					
	>=0.5 mL	161	853.5 (458.61)	152		159	824.8 (613.42)	140					
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	150	854.2 (469.44)	142		159	816.7 (615.66)	139					
	Intracranial - intraventricular hemorrhage	1	969.3 (-)	1		1	992.3 (-)	1					
	Intracranial - subdural	7	651.1 (197.36)	7		1	609.1 (-)	1					
	Intracranial - subarachnoid	7	925.3 (323.42)	6		4	969.7 (588.35)	4					
	Time to Randomization since the last FXa Inhibitor Dose												0.1496
	<8 hours	64	781.7 (323.74)	61	644.84 (64.49)	74	780.7 (848.88)	60	377.82 (63.40)	267.01 (97.20, 436.82)	0.0024	0.53 (0.17, 0.90)	
	>=8 hours	95	876.7 (501.51)	89	535.66 (42.72)	91	852.3 (303.32)	85	420.76 (45.02)	114.90 (-7.11, 236.92)	0.0648	0.28 (-0.02, 0.58)	
	Intended Usual Care Agent												0.4777
	PCC	122	831.7 (347.88)	114	578.77 (44.01)	121	828.7 (684.22)	105	419.43 (47.13)	159.34 (34.03, 284.65)	0.0130	0.33 (0.07, 0.60)	
	Other	13	1036.1 (1136.38)	13	534.69 (107.92)	8	652.1 (345.85)	8	167.99 (123.66)	366.71 (30.27, 703.15)	0.0343	0.94 (0.00, 1.87)	
	Unknown	30	839.9 (342.23)	29	598.17 (58.82)	36	829.1 (331.20)	32	391.92 (58.32)	206.25 (41.61, 370.88)	0.0151	0.63 (0.11, 1.14)	

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N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Lag Time (minutes)	Age												0.3295
	<65 years	11	6.2 (2.25)	10	-3.21 (0.30)	13	6.8 (2.47)	9	0.06 (0.31)	-3.27 (-4.19, -2.35)	<.0001	-3.37 (-4.88, -1.87)	
	65 - 74 years	34	6.0 (2.16)	31	-3.30 (0.36)	40	7.3 (3.31)	39	-0.14 (0.35)	-3.16 (-4.13, -2.18)	<.0001	-1.48 (-2.02, -0.95)	
	>=75 years	143	6.6 (3.26)	139	-3.16 (0.13)	128	6.6 (2.99)	119	-0.49 (0.14)	-2.67 (-3.04, -2.30)	<.0001	-1.78 (-2.07, -1.49)	
	Sex												0.7241
	Male	101	6.6 (3.32)	97	-3.28 (0.18)	97	7.0 (3.22)	90	-0.36 (0.19)	-2.93 (-3.44, -2.42)	<.0001	-1.63 (-1.96, -1.30)	
	Female	87	6.4 (2.68)	83	-3.10 (0.15)	84	6.6 (2.77)	77	-0.29 (0.16)	-2.81 (-3.24, -2.37)	<.0001	-1.99 (-2.37, -1.61)	
	Race												0.1086
	White	169	6.6 (3.17)	162	-3.29 (0.12)	164	6.9 (3.10)	155	-0.40 (0.13)	-2.89 (-3.23, -2.54)	<.0001	-1.82 (-2.08, -1.55)	
	Other	10	5.8 (1.00)	9	-2.59 (0.21)	15	5.5 (1.85)	11	-0.24 (0.20)	-2.34 (-2.96, -1.72)	<.0001	-3.43 (-4.91, -1.95)	
	Geographic Region 1												0.7617
	North America	18	6.9 (2.65)	16	-3.34 (0.33)	18	6.3 (2.77)	15	-0.62 (0.37)	-2.72 (-3.74, -1.71)	<.0001	-1.93 (-2.80, -1.05)	
	Europe	170	6.5 (3.08)	164	-3.19 (0.13)	163	6.9 (3.05)	152	-0.31 (0.13)	-2.88 (-3.24, -2.53)	<.0001	-1.78 (-2.04, -1.52)	
	Prior FXa Inhibitor												0.0055
	Apixaban	121	5.7 (2.08)	115	-2.67 (0.13)	120	6.5 (3.06)	113	-0.19 (0.14)	-2.48 (-2.86, -2.11)	<.0001	-1.71 (-2.01, -1.40)	
	Rivaroxaban	67	7.9 (3.91)	65	-4.18 (0.20)	61	7.5 (2.86)	54	-0.71 (0.24)	-3.47 (-4.07, -2.87)	<.0001	-2.05 (-2.50, -1.60)	
	Indication for prior FXa Inhibitor 1												0.7417
	Atrial Fibrillation/Flutter	158	6.4 (2.90)	153	-3.16 (0.13)	152	6.7 (2.90)	140	-0.24 (0.14)	-2.92 (-3.29, -2.56)	<.0001	-1.82 (-2.10, -1.55)	
	Venous Thromboembolism	20	6.7 (2.67)	18	-3.18 (0.47)	24	7.4 (3.95)	22	-0.75 (0.41)	-2.43 (-3.68, -1.18)	0.0004	-1.23 (-1.91, -0.54)	
	Other	10	7.5 (5.35)	9	-3.49 (0.25)	5	7.2 (1.56)	5	-0.59 (0.36)	-2.90 (-3.89, -1.90)	0.0001	-3.56 (-5.46, -1.66)	
	Indication for prior FXa Inhibitor 2												0.4608
	Atrial Fibrillation/Flutter	158	6.4 (2.90)	153	-3.16 (0.13)	152	6.7 (2.90)	140	-0.24 (0.14)	-2.92 (-3.29, -2.56)	<.0001	-1.82 (-2.10, -1.55)	
	Other	30	7.0 (3.70)	27	-3.29 (0.31)	29	7.3 (3.63)	27	-0.72 (0.31)	-2.57 (-3.46, -1.69)	<.0001	-1.55 (-2.17, -0.94)	
	Baseline Anti-FXa Activity 1												0.0231
	<30 ng/mL	13	3.8 (1.40)	12	-1.48 (0.25)	10	4.7 (1.50)	9	0.44 (0.34)	-1.92 (-2.81, -1.04)	0.0002	-1.98 (-3.07, -0.89)	
	>=30 ng/mL	168	6.7 (3.05)	162	-3.35 (0.13)	168	7.0 (3.04)	156	-0.39 (0.13)	-2.96 (-3.32, -2.61)	<.0001	-1.81 (-2.07, -1.55)	
	Baseline Anti-FXa Activity 2												0.0028
	<75 ng/mL	54	5.2 (1.97)	53	-2.41 (0.14)	46	5.6 (2.89)	42	-0.20 (0.16)	-2.22 (-2.64, -1.80)	<.0001	-2.14 (-2.65, -1.63)	
	>=75 ng/mL	127	7.1 (3.27)	121	-3.55 (0.16)	132	7.3 (2.95)	123	-0.43 (0.16)	-3.12 (-3.55, -2.69)	<.0001	-1.79 (-2.09, -1.50)	

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N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Lag Time (minutes)	ICH Score at baseline												0.0008
	< 3	156	6.5 (3.11)	150	-3.28 (0.13)	159	7.0 (3.13)	147	-0.30 (0.14)	-2.98 (-3.35, -2.60)	<.0001	-1.79 (-2.06, -1.52)	
	>= 3	32	6.6 (2.70)	30	-2.65 (0.15)	22	5.3 (1.35)	20	-0.72 (0.19)	-1.93 (-2.43, -1.44)	<.0001	-2.27 (-3.01, -1.54)	
	Baseline Volume of Hematoma 1												0.1029
	<30 mL	143	6.3 (2.76)	137	-3.22 (0.14)	149	6.9 (3.02)	138	-0.22 (0.15)	-3.00 (-3.40, -2.61)	<.0001	-1.77 (-2.05, -1.49)	
	>=30 mL	45	7.0 (3.76)	43	-3.10 (0.17)	31	6.0 (2.90)	28	-0.64 (0.21)	-2.46 (-2.99, -1.93)	<.0001	-2.23 (-2.84, -1.63)	
	Baseline Volume of Hematoma 2												0.2938
	<0.5 mL	4	5.5 (1.76)	4	-3.46 (3.33)	7	7.5 (3.15)	7	3.79 (4.71)	-7.25 (-18.74, 4.25)	0.1595	-0.61 (-1.88, 0.66)	
	>=0.5 mL	184	6.5 (3.06)	176	-3.19 (0.11)	173	6.7 (3.02)	159	-0.43 (0.11)	-2.75 (-3.06, -2.45)	<.0001	-1.92 (-2.18, -1.66)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	169	6.4 (2.61)	162		173	6.8 (3.03)	159					
	Intracranial - intraventricular hemorrhage	1	5.8 (-)	1		1	4.0 (-)	1					
	Intracranial - subdural	9	8.7 (5.29)	9		2	9.3 (2.12)	2					
	Intracranial - subarachnoid	9	7.1 (6.11)	8		4	5.7 (2.75)	4					
	Time to Randomization since the last FXa Inhibitor Dose												0.0581
	<8 hours	78	7.0 (3.47)	76	-3.75 (0.23)	82	7.6 (3.25)	73	-0.47 (0.24)	-3.28 (-3.90, -2.66)	<.0001	-1.64 (-2.01, -1.27)	
	>=8 hours	104	6.2 (2.68)	98	-2.84 (0.13)	99	6.2 (2.69)	94	-0.24 (0.13)	-2.59 (-2.95, -2.24)	<.0001	-2.05 (-2.40, -1.70)	
	Intended Usual Care Agent												0.0966
	PCC	139	6.5 (2.90)	132	-3.18 (0.14)	135	7.0 (3.23)	124	-0.26 (0.15)	-2.92 (-3.33, -2.51)	<.0001	-1.74 (-2.03, -1.45)	
	Other	14	7.4 (5.53)	14	-4.71 (0.21)	8	7.8 (2.72)	8	-1.39 (0.24)	-3.32 (-3.96, -2.68)	<.0001	-4.33 (-5.98, -2.67)	
	Unknown	35	6.2 (2.11)	34	-2.78 (0.20)	38	5.8 (1.97)	35	-0.36 (0.21)	-2.42 (-3.00, -1.85)	<.0001	-1.99 (-2.57, -1.40)	

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N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Peak Height (nM)	Age												0.2901
	<65 years	11	65.8 (33.75)	10	150.72 (29.26)	13	123.4 (118.48)	9	7.74 (30.01)	142.98 (53.19, 232.76)	0.0040	1.49 (0.45, 2.54)	
	65 - 74 years	34	86.3 (77.29)	31	156.07 (8.43)	40	61.3 (42.37)	39	35.29 (8.52)	120.78 (97.95, 143.61)	<.0001	2.36 (1.74, 2.98)	
	>=75 years	143	67.2 (63.89)	139	144.17 (8.91)	128	63.2 (58.05)	119	47.27 (9.64)	96.90 (71.12, 122.68)	<.0001	0.92 (0.66, 1.18)	
	Sex												0.6648
	Male	101	72.7 (67.50)	97	144.58 (6.75)	97	70.0 (67.66)	90	34.61 (7.13)	109.96 (90.98, 128.95)	<.0001	1.63 (1.30, 1.97)	
	Female	87	68.1 (63.05)	83	150.35 (12.94)	84	63.8 (57.00)	77	49.39 (13.28)	100.96 (64.31, 137.61)	<.0001	0.86 (0.53, 1.18)	
	Race												0.0101
	White	169	68.4 (67.07)	162	144.27 (7.62)	164	64.6 (62.15)	155	40.95 (7.86)	103.32 (82.02, 124.62)	<.0001	1.06 (0.82, 1.29)	
	Other	10	88.7 (44.97)	9	183.45 (8.38)	15	94.7 (69.73)	11	38.55 (8.45)	144.91 (118.75, 171.06)	<.0001	5.18 (3.19, 7.18)	
	Geographic Region 1												0.4315
	North America	18	55.1 (29.27)	16	166.71 (67.65)	18	69.9 (43.26)	15	133.58 (74.22)	33.13 (-184.39, 250.66)	0.7494	0.12 (-0.59, 0.82)	
	Europe	170	72.3 (67.90)	164	147.06 (4.98)	163	66.8 (64.74)	152	33.66 (5.23)	113.40 (99.39, 127.40)	<.0001	1.76 (1.50, 2.02)	
	Prior FXa Inhibitor												0.2603
	Apixaban	121	84.1 (74.25)	115	148.09 (10.15)	120	72.1 (62.74)	113	47.17 (10.19)	100.92 (72.62, 129.22)	<.0001	0.93 (0.65, 1.20)	
	Rivaroxaban	67	46.3 (33.80)	65	148.51 (7.31)	61	57.4 (62.43)	54	27.29 (8.64)	121.22 (99.47, 142.98)	<.0001	1.97 (1.53, 2.41)	
	Indication for prior FXa Inhibitor 1												0.4306
	Atrial Fibrillation/Flutter	158	70.7 (62.98)	153	149.87 (4.81)	152	65.8 (62.14)	140	32.08 (5.15)	117.78 (104.12, 131.45)	<.0001	1.95 (1.67, 2.23)	
	Venous Thromboembolism	20	83.3 (91.53)	18	146.29 (20.56)	24	76.5 (73.38)	22	41.11 (18.14)	105.18 (49.95, 160.42)	0.0005	1.20 (0.52, 1.88)	
	Other	10	44.0 (26.17)	9	124.20 (90.34)	5	63.8 (19.69)	5	189.46 (118.85)	-65.27 (-499.76, 369.23)	0.6874	-0.23 (-1.32, 0.87)	
	Indication for prior FXa Inhibitor 2												0.1582
	Atrial Fibrillation/Flutter	158	70.7 (62.98)	153	149.87 (4.81)	152	65.8 (62.14)	140	32.08 (5.15)	117.78 (104.12, 131.45)	<.0001	1.95 (1.67, 2.23)	
	Other	30	70.2 (77.82)	27	126.09 (44.84)	29	74.3 (67.10)	27	95.35 (42.48)	30.74 (-104.61, 166.09)	0.6261	0.13 (-0.40, 0.67)	
	Baseline Anti-FXa Activity 1												0.9523
	<30 ng/mL	13	161.5 (93.04)	12	126.30 (23.29)	10	122.6 (79.37)	9	21.25 (28.97)	105.05 (27.36, 182.74)	0.0110	1.21 (0.25, 2.16)	
	>=30 ng/mL	168	62.9 (57.53)	162	149.64 (7.70)	168	63.6 (60.83)	156	42.29 (7.87)	107.35 (85.95, 128.75)	<.0001	1.09 (0.86, 1.33)	
	Baseline Anti-FXa Activity 2												0.3711
	<75 ng/mL	54	99.2 (78.04)	53	159.80 (8.73)	46	102.4 (75.03)	42	41.99 (9.94)	117.82 (91.92, 143.71)	<.0001	1.83 (1.34, 2.31)	
	>=75 ng/mL	127	57.5 (55.29)	121	142.16 (9.06)	132	54.6 (53.56)	123	40.59 (9.05)	101.56 (76.52, 126.61)	<.0001	1.01 (0.75, 1.28)	

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SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.3.3.1
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Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Peak Height (nM)	ICH Score at baseline												0.8267
	< 3	156	72.1 (65.98)	150	147.52 (8.14)	159	67.2 (66.22)	147	40.65 (8.28)	106.87 (84.23, 129.51)	<.0001	1.06 (0.82, 1.31)	
	>= 3	32	63.4 (62.65)	30	143.85 (11.51)	22	66.5 (29.32)	20	41.69 (14.34)	102.16 (65.50, 138.83)	<.0001	1.58 (0.93, 2.24)	
	Baseline Volume of Hematoma 1												0.9278
	<30 mL	143	70.3 (67.40)	137	144.92 (8.61)	149	67.6 (66.26)	138	39.84 (8.62)	105.08 (81.33, 128.83)	<.0001	1.04 (0.79, 1.29)	
	>=30 mL	45	71.5 (59.05)	43	154.21 (10.23)	31	66.8 (43.67)	28	47.30 (12.86)	106.92 (74.31, 139.52)	<.0001	1.57 (1.02, 2.11)	
	Baseline Volume of Hematoma 2												0.6689
	<0.5 mL	4	82.3 (92.84)	4	109.79 (42.79)	7	57.1 (63.54)	7	-20.02 (58.71)	129.81 (-5.57, 265.19)	0.0574	0.87 (-0.44, 2.18)	
	>=0.5 mL	184	70.4 (64.95)	176	147.90 (7.32)	173	67.9 (62.96)	159	42.31 (7.72)	105.59 (84.84, 126.34)	<.0001	1.08 (0.85, 1.31)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	169	71.7 (66.75)	162		173	66.6 (61.40)	159					
	Intracranial - intraventricular hemorrhage	1	75.2 (-)	1		1	112.0 (-)	1					
	Intracranial - subdural	9	40.8 (23.99)	9		2	29.9 (21.45)	2					
	Intracranial - subarachnoid	9	79.7 (67.33)	8		4	115.2 (121.20)	4					
	Time to Randomization since the last FXa Inhibitor Dose												0.6504
	<8 hours	78	62.9 (59.73)	76	148.39 (14.35)	82	55.7 (61.53)	73	46.52 (14.68)	101.87 (61.87, 141.86)	<.0001	0.81 (0.47, 1.14)	
	>=8 hours	104	73.3 (63.89)	98	148.55 (5.78)	99	76.6 (62.65)	94	36.81 (5.93)	111.74 (95.51, 127.96)	<.0001	1.94 (1.60, 2.28)	
	Intended Usual Care Agent												0.2744
	PCC	139	69.5 (61.11)	132	144.79 (9.72)	135	68.9 (67.74)	124	42.89 (10.07)	101.89 (74.56, 129.22)	<.0001	0.91 (0.65, 1.17)	
	Other	14	95.7 (122.21)	14	140.89 (21.30)	8	42.9 (24.05)	8	42.22 (26.54)	98.68 (28.67, 168.68)	0.0081	1.22 (0.26, 2.17)	
	Unknown	35	65.2 (48.19)	34	163.58 (6.66)	38	65.9 (48.40)	35	36.66 (6.85)	126.92 (108.09, 145.75)	<.0001	3.16 (2.44, 3.88)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N Mean (SD)	Andexanet (N=241) Change from BL N LSMean (SE)	Usual Care (N=233) Baseline N Mean (SD)	Usual Care (N=233) Change from BL N LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Time to Peak (minutes)	Age								0.7282
	<65 years	11 11.0 (4.06)	10 -5.36 (0.74)	13 12.2 (4.91)	9 1.34 (0.78)	-6.70 (-9.02, -4.38)	<.0001	-2.73 (-4.05, -1.40)	
	65 - 74 years	34 12.3 (5.33)	31 -6.26 (0.72)	40 14.7 (7.62)	39 0.21 (0.71)	-6.47 (-8.42, -4.52)	<.0001	-1.50 (-2.04, -0.97)	
	>=75 years	143 13.2 (6.92)	139 -5.53 (0.31)	128 12.1 (5.47)	119 0.37 (0.34)	-5.90 (-6.81, -4.99)	<.0001	-1.59 (-1.87, -1.31)	
	Sex								0.7078
	Male	101 13.1 (7.38)	97 -5.86 (0.40)	97 13.1 (6.24)	90 0.41 (0.42)	-6.27 (-7.39, -5.15)	<.0001	-1.59 (-1.92, -1.26)	
	Female	87 12.7 (5.39)	83 -5.44 (0.39)	84 12.3 (5.81)	77 0.53 (0.42)	-5.97 (-7.09, -4.85)	<.0001	-1.65 (-2.01, -1.29)	
	Race								0.1040
	White	169 13.1 (6.76)	162 -5.77 (0.29)	164 12.8 (6.14)	155 0.36 (0.30)	-6.13 (-6.95, -5.31)	<.0001	-1.64 (-1.89, -1.38)	
	Other	10 11.0 (2.44)	9 -5.03 (0.49)	15 11.3 (5.27)	11 -0.18 (0.46)	-4.85 (-6.28, -3.41)	<.0001	-3.09 (-4.48, -1.71)	
	Geographic Region 1								0.6146
	North America	18 12.6 (5.40)	16 -5.46 (0.66)	18 10.7 (4.44)	15 0.19 (0.75)	-5.65 (-7.72, -3.58)	<.0001	-1.99 (-2.88, -1.11)	
	Europe	170 13.0 (6.64)	164 -5.71 (0.29)	163 12.9 (6.16)	152 0.49 (0.31)	-6.20 (-7.03, -5.36)	<.0001	-1.63 (-1.88, -1.37)	
	Prior FXa Inhibitor								0.0008
	Apixaban	121 10.1 (4.44)	115 -3.78 (0.34)	120 10.5 (4.88)	113 1.46 (0.35)	-5.24 (-6.19, -4.28)	<.0001	-1.43 (-1.72, -1.13)	
	Rivaroxaban	67 18.0 (6.66)	65 -9.38 (0.42)	61 17.1 (5.72)	54 -1.50 (0.49)	-7.88 (-9.12, -6.65)	<.0001	-2.25 (-2.71, -1.78)	
	Indication for prior FXa Inhibitor 1								0.6392
	Atrial Fibrillation/Flutter	158 12.7 (6.32)	153 -5.60 (0.29)	152 12.4 (5.74)	140 0.60 (0.31)	-6.20 (-7.02, -5.38)	<.0001	-1.72 (-1.99, -1.46)	
	Venous Thromboembolism	20 13.0 (5.90)	18 -5.33 (1.23)	24 14.3 (7.73)	22 0.17 (1.12)	-5.50 (-8.88, -2.12)	0.0023	-1.03 (-1.70, -0.36)	
	Other	10 16.3 (10.05)	9 -6.61 (0.67)	5 14.6 (5.41)	5 0.61 (0.97)	-7.22 (-9.92, -4.52)	0.0002	-3.28 (-5.09, -1.48)	
	Indication for prior FXa Inhibitor 2								0.8499
	Atrial Fibrillation/Flutter	158 12.7 (6.32)	153 -5.60 (0.29)	152 12.4 (5.74)	140 0.60 (0.31)	-6.20 (-7.02, -5.38)	<.0001	-1.72 (-1.99, -1.46)	
	Other	30 14.1 (7.53)	27 -5.88 (0.86)	29 14.3 (7.30)	27 0.08 (0.87)	-5.96 (-8.41, -3.51)	<.0001	-1.31 (-1.90, -0.71)	
	Baseline Anti-FXa Activity 1								0.3665
	<30 ng/mL	13 7.5 (2.15)	12 -2.98 (0.78)	10 8.8 (3.27)	9 2.06 (1.01)	-5.03 (-7.71, -2.36)	0.0009	-1.70 (-2.74, -0.66)	
	>=30 ng/mL	168 13.4 (6.54)	162 -5.88 (0.30)	168 13.0 (6.11)	156 0.36 (0.31)	-6.25 (-7.08, -5.42)	<.0001	-1.64 (-1.89, -1.38)	
	Baseline Anti-FXa Activity 2								0.0323
	<75 ng/mL	54 10.1 (3.78)	53 -4.55 (0.35)	46 10.5 (5.91)	42 0.40 (0.40)	-4.95 (-5.99, -3.92)	<.0001	-1.93 (-2.42, -1.44)	
	>=75 ng/mL	127 14.1 (7.04)	121 -6.12 (0.36)	132 13.6 (5.94)	123 0.39 (0.37)	-6.52 (-7.52, -5.51)	<.0001	-1.60 (-1.89, -1.31)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Time to Peak (minutes)	ICH Score at baseline												0.6486
	< 3	156	13.0 (6.76)	150	-5.75 (0.31)	159	13.0 (6.17)	147	0.41 (0.32)	-6.16 (-7.03, -5.30)	<.0001	-1.60 (-1.86, -1.34)	
	>= 3	32	12.6 (5.31)	30	-5.08 (0.50)	22	10.7 (4.61)	20	0.65 (0.65)	-5.73 (-7.40, -4.07)	<.0001	-2.00 (-2.70, -1.30)	
	Baseline Volume of Hematoma 1												0.1577
	<30 mL	143	12.9 (6.40)	137	-5.75 (0.33)	149	12.9 (6.07)	138	0.66 (0.34)	-6.41 (-7.33, -5.50)	<.0001	-1.63 (-1.91, -1.36)	
	>=30 mL	45	12.9 (6.97)	43	-5.28 (0.38)	31	11.0 (5.08)	28	0.04 (0.49)	-5.32 (-6.56, -4.08)	<.0001	-2.07 (-2.66, -1.48)	
	Baseline Volume of Hematoma 2												0.2549
	<0.5 mL	4	10.4 (3.84)	4	-6.29 (5.46)	7	13.9 (5.34)	7	7.80 (7.37)	-14.09 (-33.67, 5.49)	0.1173	-0.75 (-2.04, 0.54)	
	>=0.5 mL	184	13.0 (6.57)	176	-5.64 (0.26)	173	12.6 (5.98)	159	0.33 (0.28)	-5.97 (-6.71, -5.23)	<.0001	-1.72 (-1.98, -1.47)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	169	12.8 (6.20)	162		173	12.7 (5.99)	159					
	Intracranial - intraventricular hemorrhage	1	13.9 (-)	1		1	6.8 (-)	1					
	Intracranial - subdural	9	14.6 (10.09)	9		2	12.9 (2.52)	2					
	Intracranial - subarachnoid	9	12.8 (9.13)	8		4	10.0 (5.05)	4					
	Time to Randomization since the last FXa Inhibitor Dose												0.5932
	<8 hours	78	13.5 (6.83)	76	-6.29 (0.45)	82	14.3 (6.74)	73	0.15 (0.47)	-6.43 (-7.69, -5.18)	<.0001	-1.60 (-1.97, -1.23)	
	>=8 hours	104	12.6 (6.37)	98	-5.25 (0.36)	99	11.4 (5.05)	94	0.75 (0.37)	-6.00 (-7.00, -4.99)	<.0001	-1.69 (-2.02, -1.36)	
	Intended Usual Care Agent												0.9180
	PCC	139	13.0 (6.55)	132	-5.65 (0.34)	135	13.1 (6.46)	124	0.61 (0.36)	-6.26 (-7.23, -5.29)	<.0001	-1.57 (-1.85, -1.28)	
	Other	14	13.2 (8.94)	14	-7.71 (0.56)	8	14.2 (4.61)	8	-1.62 (0.67)	-6.09 (-7.87, -4.31)	<.0001	-2.88 (-4.16, -1.60)	
	Unknown	35	12.4 (5.42)	34	-5.41 (0.50)	38	10.9 (4.24)	35	0.49 (0.52)	-5.90 (-7.35, -4.45)	<.0001	-1.94 (-2.51, -1.36)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Velocity Index (nM/min)	Age												0.1054
	<65 years	11	17.6 (10.85)	10	77.64 (7.79)	13	30.0 (31.28)	9	0.19 (8.12)	77.45 (53.60, 101.30)	<.0001	3.02 (1.61, 4.42)	
	65 - 74 years	34	25.4 (39.11)	31	66.90 (4.57)	40	14.7 (16.19)	39	5.29 (4.58)	61.61 (49.18, 74.05)	<.0001	2.24 (1.63, 2.84)	
	>=75 years	143	18.6 (28.57)	139	61.67 (7.70)	128	19.3 (32.27)	119	17.92 (8.35)	43.75 (21.40, 66.11)	0.0002	0.48 (0.23, 0.73)	
	Sex												0.4042
	Male	101	20.8 (31.52)	97	64.54 (3.52)	97	19.5 (32.60)	90	7.89 (3.72)	56.65 (46.76, 66.55)	<.0001	1.61 (1.28, 1.95)	
	Female	87	18.5 (28.38)	83	64.18 (11.62)	84	18.5 (25.61)	77	21.94 (11.84)	42.23 (9.36, 75.11)	0.0124	0.40 (0.09, 0.71)	
	Race												0.0071
	White	169	19.4 (31.25)	162	62.11 (6.44)	164	18.5 (30.09)	155	14.36 (6.62)	47.75 (29.64, 65.85)	<.0001	0.58 (0.35, 0.80)	
	Other	10	21.1 (15.77)	9	91.50 (5.96)	15	24.7 (24.37)	11	10.04 (5.92)	81.46 (63.32, 99.60)	<.0001	4.13 (2.45, 5.81)	
	Geographic Region 1												0.3941
	North America	18	14.5 (10.93)	16	74.31 (53.73)	18	20.8 (15.01)	15	82.49 (55.68)	-8.18 (-167.93, 151.57)	0.9167	-0.04 (-0.74, 0.67)	
	Europe	170	20.3 (31.37)	164	65.03 (2.61)	163	18.8 (30.70)	152	7.14 (2.74)	57.89 (50.55, 65.23)	<.0001	1.72 (1.46, 1.98)	
	Prior FXa Inhibitor												0.4995
	Apixaban	121	26.8 (34.92)	115	65.77 (8.84)	120	23.7 (33.21)	113	17.72 (8.90)	48.05 (23.30, 72.81)	0.0002	0.51 (0.24, 0.77)	
	Rivaroxaban	67	6.9 (9.12)	65	63.02 (3.54)	61	9.7 (16.98)	54	5.77 (4.21)	57.24 (46.68, 67.81)	<.0001	1.92 (1.48, 2.36)	
	Indication for prior FXa Inhibitor 1												0.3617
	Atrial Fibrillation/Flutter	158	19.9 (30.25)	153	66.80 (2.56)	152	18.7 (29.96)	140	6.34 (2.74)	60.46 (53.18, 67.74)	<.0001	1.88 (1.60, 2.16)	
	Venous Thromboembolism	20	23.3 (34.83)	18	58.48 (9.05)	24	22.4 (29.59)	22	9.48 (8.03)	48.99 (24.64, 73.34)	0.0002	1.26 (0.58, 1.95)	
	Other	10	9.8 (10.43)	9	NE	5	12.7 (9.54)	5	NE	NE		NE	
	Indication for prior FXa Inhibitor 2												0.1807
	Atrial Fibrillation/Flutter	158	19.9 (30.25)	153	66.80 (2.56)	152	18.7 (29.96)	140	6.34 (2.74)	60.46 (53.18, 67.74)	<.0001	1.88 (1.60, 2.16)	
	Other	30	18.8 (29.50)	27	50.29 (35.91)	29	20.7 (27.32)	27	56.10 (34.21)	-5.81 (-109.94, 98.31)	0.9076	-0.03 (-0.56, 0.50)	
	Baseline Anti-FXa Activity 1												0.1605
	<30 ng/mL	13	54.0 (40.65)	12	72.91 (11.00)	10	37.2 (27.57)	9	-3.63 (13.75)	76.54 (39.80, 113.28)	0.0004	1.86 (0.80, 2.93)	
	>=30 ng/mL	168	16.9 (27.84)	162	63.84 (6.47)	168	17.9 (29.57)	156	14.96 (6.60)	48.88 (30.78, 66.97)	<.0001	0.59 (0.37, 0.82)	
	Baseline Anti-FXa Activity 2												0.0279
	<75 ng/mL	54	30.5 (37.01)	53	79.32 (3.86)	46	27.7 (22.35)	42	9.62 (4.42)	69.70 (58.24, 81.16)	<.0001	2.44 (1.90, 2.98)	
	>=75 ng/mL	127	14.9 (25.83)	121	57.78 (8.08)	132	16.0 (31.41)	123	16.04 (8.04)	41.74 (19.34, 64.14)	0.0003	0.47 (0.21, 0.72)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.3.3.1
MMRM Analysis of Change From Baseline in Thrombin Generation Parameters by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
ETP Velocity Index (nM/min)	ICH Score at baseline												0.6487
	< 3	156	20.4 (31.39)	150	63.77 (6.92)	159	19.2 (31.13)	147	14.51 (7.02)	49.26 (29.92, 68.60)	<.0001	0.58 (0.35, 0.81)	
	>= 3	32	16.8 (22.60)	30	62.45 (5.86)	22	18.1 (12.74)	20	7.06 (7.24)	55.39 (36.85, 73.92)	<.0001	1.69 (1.03, 2.36)	
	Baseline Volume of Hematoma 1												0.4915
	<30 mL	143	19.9 (32.52)	137	62.82 (7.40)	149	19.2 (31.64)	138	14.39 (7.38)	48.43 (27.92, 68.95)	<.0001	0.56 (0.32, 0.80)	
	>=30 mL	45	19.2 (20.63)	43	68.20 (5.24)	31	18.8 (16.31)	28	10.60 (6.56)	57.60 (40.94, 74.27)	<.0001	1.65 (1.10, 2.20)	
	Baseline Volume of Hematoma 2												0.8944
	<0.5 mL	4	30.0 (43.29)	4	47.28 (10.21)	7	14.2 (21.97)	7	-4.61 (16.02)	51.89 (12.56, 91.22)	0.0201	1.30 (-0.11, 2.70)	
	>=0.5 mL	184	19.5 (29.83)	176	64.23 (6.19)	173	19.3 (29.83)	159	14.65 (6.52)	49.58 (31.95, 67.22)	<.0001	0.60 (0.38, 0.82)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	169	20.1 (30.90)	162		173	18.7 (29.42)	159					
	Intracranial - intraventricular hemorrhage	1	9.3 (-)	1		1	40.7 (-)	1					
	Intracranial - subdural	9	10.7 (8.06)	9		2	8.7 (6.88)	2					
	Intracranial - subarachnoid	9	23.9 (29.42)	8		4	36.5 (42.04)	4					
	Time to Randomization since the last FXa Inhibitor Dose												0.2067
	<8 hours	78	17.7 (28.79)	76	61.53 (12.56)	82	14.1 (23.20)	73	24.67 (12.84)	36.87 (1.51, 72.23)	0.0411	0.33 (0.01, 0.66)	
	>=8 hours	104	20.1 (29.84)	98	66.81 (3.16)	99	23.1 (33.39)	94	6.70 (3.24)	60.11 (51.24, 68.98)	<.0001	1.91 (1.57, 2.25)	
	Intended Usual Care Agent												0.1268
	PCC	139	18.8 (26.72)	132	62.21 (8.21)	135	20.0 (32.84)	124	15.62 (8.48)	46.59 (23.38, 69.80)	0.0001	0.49 (0.24, 0.74)	
	Other	14	36.7 (66.19)	14	57.97 (12.36)	8	8.9 (5.90)	8	18.53 (15.59)	39.44 (-1.54, 80.42)	0.0584	0.83 (-0.08, 1.74)	
	Unknown	35	16.7 (16.19)	34	75.45 (3.67)	38	17.9 (17.09)	35	7.96 (3.76)	67.49 (57.11, 77.87)	<.0001	3.05 (2.35, 3.76)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.4.1
Proportion of Participants with Neurologic Deterioration at 24 hours post-randomization (NRI)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	47/241 (19.5)	45/233 (19.3)
Number of missing values	0	0
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.02 (0.71, 1.46)	
p-value	0.9273	
Odds Ratio (95% CI)	1.02 (0.65, 1.62)	
p-value	0.9274	
Risk Difference (95% CI)	0.33 (-6.74, 7.40)	
p-value	0.9274	
p-value of CMH-Test	0.9273	
p-value of Breslow-Day Test	0.1182	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.1.1
Proportion of Participants with Neurologic Deterioration at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.3109
<65 years	1/ 13 (7.7)	2/ 16 (12.5)	0.65 (0.08, 5.45)	0.6946	
65 - 74 years	12/ 45 (26.7)	9/ 51 (17.6)	1.66 (0.81, 3.40)	0.1685	
>=75 years	34/ 183 (18.6)	34/ 166 (20.5)	0.89 (0.58, 1.35)	0.5786	
Sex					0.2836
Male	25/ 130 (19.2)	27/ 118 (22.9)	0.85 (0.53, 1.37)	0.5064	
Female	22/ 111 (19.8)	18/ 115 (15.7)	1.27 (0.73, 2.22)	0.3994	
Race					0.8583
White	41/ 217 (18.9)	41/ 213 (19.2)	0.99 (0.67, 1.45)	0.9552	
Other	3/ 15 (20.0)	3/ 16 (18.8)	1.13 (0.28, 4.64)	0.8652	
Geographic Region 1					0.0889
North America	3/ 29 (10.3)	9/ 27 (33.3)	0.42 (0.14, 1.29)	0.1305	
Europe	44/ 212 (20.8)	36/ 206 (17.5)	1.18 (0.79, 1.76)	0.4089	
Prior FXa Inhibitor					0.0853
Apixaban	25/ 162 (15.4)	31/ 158 (19.6)	0.78 (0.49, 1.25)	0.3028	
Rivaroxaban	22/ 79 (27.8)	14/ 75 (18.7)	1.51 (0.84, 2.72)	0.1677	
Indication for prior FXa Inhibitor 1					0.0553
Atrial Fibrillation/Flutter	35/ 208 (16.8)	40/ 194 (20.6)	0.83 (0.56, 1.25)	0.3728	
Venous Thromboembolism	7/ 20 (35.0)	4/ 31 (12.9)	2.98 (0.97, 9.15)	0.0564	
Other	5/ 13 (38.5)	1/ 8 (12.5)	3.29 (0.44, 24.33)	0.2442	
Indication for prior FXa Inhibitor 2					0.0177
Atrial Fibrillation/Flutter	35/ 208 (16.8)	40/ 194 (20.6)	0.83 (0.56, 1.25)	0.3728	
Other	12/ 33 (36.4)	5/ 39 (12.8)	2.86 (1.12, 7.29)	0.0279	
Baseline Anti-FXa Activity 1					0.9655
<30 ng/mL	4/ 15 (26.7)	3/ 11 (27.3)	0.93 (0.30, 2.93)	0.9059	
>=30 ng/mL	41/ 211 (19.4)	41/ 202 (20.3)	0.96 (0.65, 1.41)	0.8296	
Baseline Anti-FXa Activity 2					0.3864
<75 ng/mL	16/ 67 (23.9)	10/ 52 (19.2)	1.24 (0.62, 2.48)	0.5416	
>=75 ng/mL	29/ 159 (18.2)	34/ 161 (21.1)	0.86 (0.55, 1.34)	0.5132	
ICH Score at baseline					0.3608
< 3	38/ 203 (18.7)	35/ 204 (17.2)	1.09 (0.72, 1.65)	0.6851	
>= 3	9/ 38 (23.7)	10/ 29 (34.5)	0.74 (0.35, 1.53)	0.4120	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 2.4.1.1
Proportion of Participants with Neurologic Deterioration at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.2844
<30 mL	32/ 190 (16.8)	29/ 193 (15.0)	1.13 (0.72, 1.79)	0.5981	
>=30 mL	15/ 51 (29.4)	15/ 39 (38.5)	0.75 (0.42, 1.35)	0.3437	
Baseline Volume of Hematoma 2					0.7781
<0.5 mL	0/ 7 (0.0)	1/ 11 (9.1)	0.67 (0.03, 13.60)	0.7921	
>=0.5 mL	47/ 234 (20.1)	43/ 221 (19.5)	1.03 (0.71, 1.49)	0.8673	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	46/ 215 (21.4)	44/ 218 (20.2)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 13 (7.7)	0/ 5 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.1950
<8 hours	19/ 101 (18.8)	26/ 103 (25.2)	0.78 (0.47, 1.29)	0.3293	
>=8 hours	25/ 133 (18.8)	19/ 130 (14.6)	1.28 (0.73, 2.22)	0.3879	
Intended Usual Care Agent					0.7109
PCC	44/ 160 (27.5)	42/ 156 (26.9)	1.02 (0.71, 1.46)	0.9257	
Other	3/ 18 (16.7)	2/ 11 (18.2)	0.81 (0.17, 3.75)	0.7851	
Unknown	0/ 63 (0.0)	1/ 66 (1.5)	0.29 (0.01, 6.76)	0.4376	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.2
Proportion of Participants with NIHSS score increase >=4 at 24 hours post-randomization (NRI)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	28/241 (11.6)	37/233 (15.9)
Number of missing values	0	0
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.74 (0.47, 1.16)	
p-value	0.1864	
Odds Ratio (95% CI)	0.70 (0.41, 1.19)	
p-value	0.1861	
Risk Difference (95% CI)	-4.18 (-10.36, 2.00)	
p-value	0.1845	
p-value of CMH-Test	0.1847	
p-value of Breslow-Day Test	0.2740	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.2.1
Proportion of Participants with NIHSS score increase >=4 at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.8858
<65 years	1/ 13 (7.7)	1/ 16 (6.3)	1.12 (0.11, 11.93)	0.9250	
65 - 74 years	6/ 45 (13.3)	9/ 51 (17.6)	0.83 (0.34, 2.03)	0.6799	
>=75 years	21/ 183 (11.5)	27/ 166 (16.3)	0.69 (0.41, 1.17)	0.1701	
Sex					0.1335
Male	15/ 130 (11.5)	25/ 118 (21.2)	0.55 (0.31, 0.99)	0.0453	
Female	13/ 111 (11.7)	12/ 115 (10.4)	1.13 (0.54, 2.35)	0.7488	
Race					0.2938
White	26/ 217 (12.0)	36/ 213 (16.9)	0.71 (0.45, 1.14)	0.1545	
Other	1/ 15 (6.7)	0/ 16 (0.0)	3.75 (0.18, 80.19)	0.3976	
Geographic Region 1					0.4009
North America	1/ 29 (3.4)	4/ 27 (14.8)	0.32 (0.04, 2.55)	0.2795	
Europe	27/ 212 (12.7)	33/ 206 (16.0)	0.79 (0.49, 1.27)	0.3299	
Prior FXa Inhibitor					0.2067
Apixaban	15/ 162 (9.3)	25/ 158 (15.8)	0.58 (0.32, 1.06)	0.0769	
Rivaroxaban	13/ 79 (16.5)	12/ 75 (16.0)	1.06 (0.52, 2.15)	0.8746	
Indication for prior FXa Inhibitor 1					0.0068
Atrial Fibrillation/Flutter	18/ 208 (8.7)	34/ 194 (17.5)	0.50 (0.30, 0.86)	0.0114	
Venous Thromboembolism	6/ 20 (30.0)	3/ 31 (9.7)	3.84 (1.01, 14.55)	0.0481	
Other	4/ 13 (30.8)	0/ 8 (0.0)	3.26 (0.45, 23.81)	0.2436	
Indication for prior FXa Inhibitor 2					0.0018
Atrial Fibrillation/Flutter	18/ 208 (8.7)	34/ 194 (17.5)	0.50 (0.30, 0.86)	0.0114	
Other	10/ 33 (30.3)	3/ 39 (7.7)	4.24 (1.25, 14.39)	0.0206	
Baseline Anti-FXa Activity 1					0.9699
<30 ng/mL	2/ 15 (13.3)	2/ 11 (18.2)	0.70 (0.13, 3.85)	0.6819	
>=30 ng/mL	24/ 211 (11.4)	34/ 202 (16.8)	0.68 (0.42, 1.10)	0.1139	
Baseline Anti-FXa Activity 2					0.7447
<75 ng/mL	8/ 67 (11.9)	8/ 52 (15.4)	0.78 (0.31, 1.93)	0.5844	
>=75 ng/mL	18/ 159 (11.3)	28/ 161 (17.4)	0.65 (0.38, 1.13)	0.1239	
ICH Score at baseline					0.0778
< 3	24/ 203 (11.8)	27/ 204 (13.2)	0.89 (0.53, 1.49)	0.6608	
>= 3	4/ 38 (10.5)	10/ 29 (34.5)	0.32 (0.11, 0.89)	0.0287	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.2.1
Proportion of Participants with NIHSS score increase >=4 at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.1154
<30 mL	20/ 190 (10.5)	22/ 193 (11.4)	0.93 (0.53, 1.64)	0.8037	
>=30 mL	8/ 51 (15.7)	14/ 39 (35.9)	0.43 (0.20, 0.93)	0.0325	
Baseline Volume of Hematoma 2					0.9361
<0.5 mL	0/ 7 (0.0)	1/ 11 (9.1)	0.67 (0.03, 13.60)	0.7921	
>=0.5 mL	28/ 234 (12.0)	35/ 221 (15.8)	0.76 (0.48, 1.20)	0.2319	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	27/ 215 (12.6)	36/ 218 (16.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 13 (7.7)	0/ 5 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.7659
<8 hours	15/ 101 (14.9)	20/ 103 (19.4)	0.79 (0.43, 1.44)	0.4425	
>=8 hours	12/ 133 (9.0)	17/ 130 (13.1)	0.69 (0.34, 1.39)	0.2937	
Intended Usual Care Agent					0.7109
PCC	26/ 160 (16.3)	36/ 156 (23.1)	0.70 (0.45, 1.10)	0.1260	
Other	2/ 18 (11.1)	1/ 11 (9.1)	1.08 (0.12, 9.89)	0.9478	
Unknown	0/ 63 (0.0)	0/ 66 (0.0)	NE		

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.3
Proportion of Participants with GCS score decrease >=2 at 24 hours post-randomization (NRI)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	38/241 (15.8)	35/233 (15.0)
Number of missing values	0	0
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.06 (0.69, 1.61)	
p-value	0.7969	
Odds Ratio (95% CI)	1.07 (0.65, 1.76)	
p-value	0.7970	
Risk Difference (95% CI)	0.85 (-5.62, 7.32)	
p-value	0.7969	
p-value of CMH-Test	0.7970	
p-value of Breslow-Day Test	0.2329	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.4.3.1
Proportion of Participants with GCS score decrease >=2 at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.3799
<65 years	0/ 13 (0.0)	2/ 16 (12.5)	0.38 (0.04, 3.23)	0.3722	
65 - 74 years	9/ 45 (20.0)	7/ 51 (13.7)	1.62 (0.70, 3.80)	0.2623	
>=75 years	29/ 183 (15.8)	26/ 166 (15.7)	0.99 (0.61, 1.61)	0.9723	
Sex					0.3153
Male	21/ 130 (16.2)	22/ 118 (18.6)	0.88 (0.51, 1.50)	0.6293	
Female	17/ 111 (15.3)	13/ 115 (11.3)	1.36 (0.70, 2.65)	0.3677	
Race					0.6780
White	33/ 217 (15.2)	31/ 213 (14.6)	1.05 (0.67, 1.65)	0.8225	
Other	2/ 15 (13.3)	3/ 16 (18.8)	0.73 (0.14, 3.86)	0.7118	
Geographic Region 1					0.0685
North America	3/ 29 (10.3)	9/ 27 (33.3)	0.42 (0.14, 1.29)	0.1305	
Europe	35/ 212 (16.5)	26/ 206 (12.6)	1.30 (0.81, 2.09)	0.2703	
Prior FXa Inhibitor					0.8480
Apixaban	23/ 162 (14.2)	22/ 158 (13.9)	1.01 (0.59, 1.73)	0.9683	
Rivaroxaban	15/ 79 (19.0)	13/ 75 (17.3)	1.10 (0.56, 2.14)	0.7812	
Indication for prior FXa Inhibitor 1					0.6481
Atrial Fibrillation/Flutter	31/ 208 (14.9)	30/ 194 (15.5)	0.98 (0.62, 1.55)	0.9394	
Venous Thromboembolism	3/ 20 (15.0)	4/ 31 (12.9)	1.30 (0.32, 5.24)	0.7141	
Other	4/ 13 (30.8)	1/ 8 (12.5)	2.57 (0.31, 21.05)	0.3786	
Indication for prior FXa Inhibitor 2					0.3470
Atrial Fibrillation/Flutter	31/ 208 (14.9)	30/ 194 (15.5)	0.98 (0.62, 1.55)	0.9394	
Other	7/ 33 (21.2)	5/ 39 (12.8)	1.69 (0.60, 4.79)	0.3204	
Baseline Anti-FXa Activity 1					0.9399
<30 ng/mL	3/ 15 (20.0)	2/ 11 (18.2)	1.05 (0.23, 4.73)	0.9494	
>=30 ng/mL	33/ 211 (15.6)	32/ 202 (15.8)	0.99 (0.63, 1.54)	0.9590	
Baseline Anti-FXa Activity 2					0.4772
<75 ng/mL	13/ 67 (19.4)	8/ 52 (15.4)	1.26 (0.57, 2.78)	0.5659	
>=75 ng/mL	23/ 159 (14.5)	26/ 161 (16.1)	0.90 (0.53, 1.50)	0.6738	
ICH Score at baseline					0.8086
< 3	30/ 203 (14.8)	28/ 204 (13.7)	1.08 (0.67, 1.73)	0.7648	
>= 3	8/ 38 (21.1)	7/ 29 (24.1)	0.95 (0.40, 2.24)	0.9116	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 2.4.3.1
Proportion of Participants with GCS score decrease >=2 at 24 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9440
<30 mL	24/ 190 (12.6)	24/ 193 (12.4)	1.02 (0.60, 1.73)	0.9330	
>=30 mL	14/ 51 (27.5)	10/ 39 (25.6)	1.06 (0.52, 2.13)	0.8797	
Baseline Volume of Hematoma 2					0.7530
<0.5 mL	0/ 7 (0.0)	1/ 11 (9.1)	0.67 (0.03, 13.60)	0.7921	
>=0.5 mL	38/ 234 (16.2)	33/ 221 (14.9)	1.09 (0.71, 1.67)	0.7012	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	37/ 215 (17.2)	34/ 218 (15.6)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 13 (7.7)	0/ 5 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.0352
<8 hours	13/ 101 (12.9)	22/ 103 (21.4)	0.63 (0.34, 1.16)	0.1377	
>=8 hours	22/ 133 (16.5)	13/ 130 (10.0)	1.65 (0.86, 3.18)	0.1349	
Intended Usual Care Agent					0.6886
PCC	35/ 160 (21.9)	32/ 156 (20.5)	1.06 (0.70, 1.62)	0.7792	
Other	3/ 18 (16.7)	2/ 11 (18.2)	0.81 (0.17, 3.75)	0.7851	
Unknown	0/ 63 (0.0)	1/ 66 (1.5)	0.29 (0.01, 6.76)	0.4376	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.1
Completion Rates for National Institutes of Health Stroke Scale (NIHSS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) n/ N	Andexanet (N=241) Completion rate	Usual Care (N=233) n/ N	Usual Care (N=233) Completion rate
Total Score NIHSS	Baseline	239/ 241	99.17%	231/ 233	99.14%
	2 Hours Post Randomization	156/ 241	64.73%	159/ 233	68.24%
	3 Hours Post Randomization	223/ 241	92.53%	227/ 232	97.84%
	6 Hours Post Randomization	220/ 240	91.67%	220/ 232	94.83%
	12 Hours Post Randomization	225/ 239	94.14%	222/ 231	96.10%
	24 Hours Post Randomization	151/ 236	63.98%	152/ 226	67.26%
	72 Hours Post Randomization	143/ 228	62.72%	142/ 217	65.44%

n describes number of patients with non-missing value at the respective timepoint.
N defines number of patients still alive at beginning of visit window.

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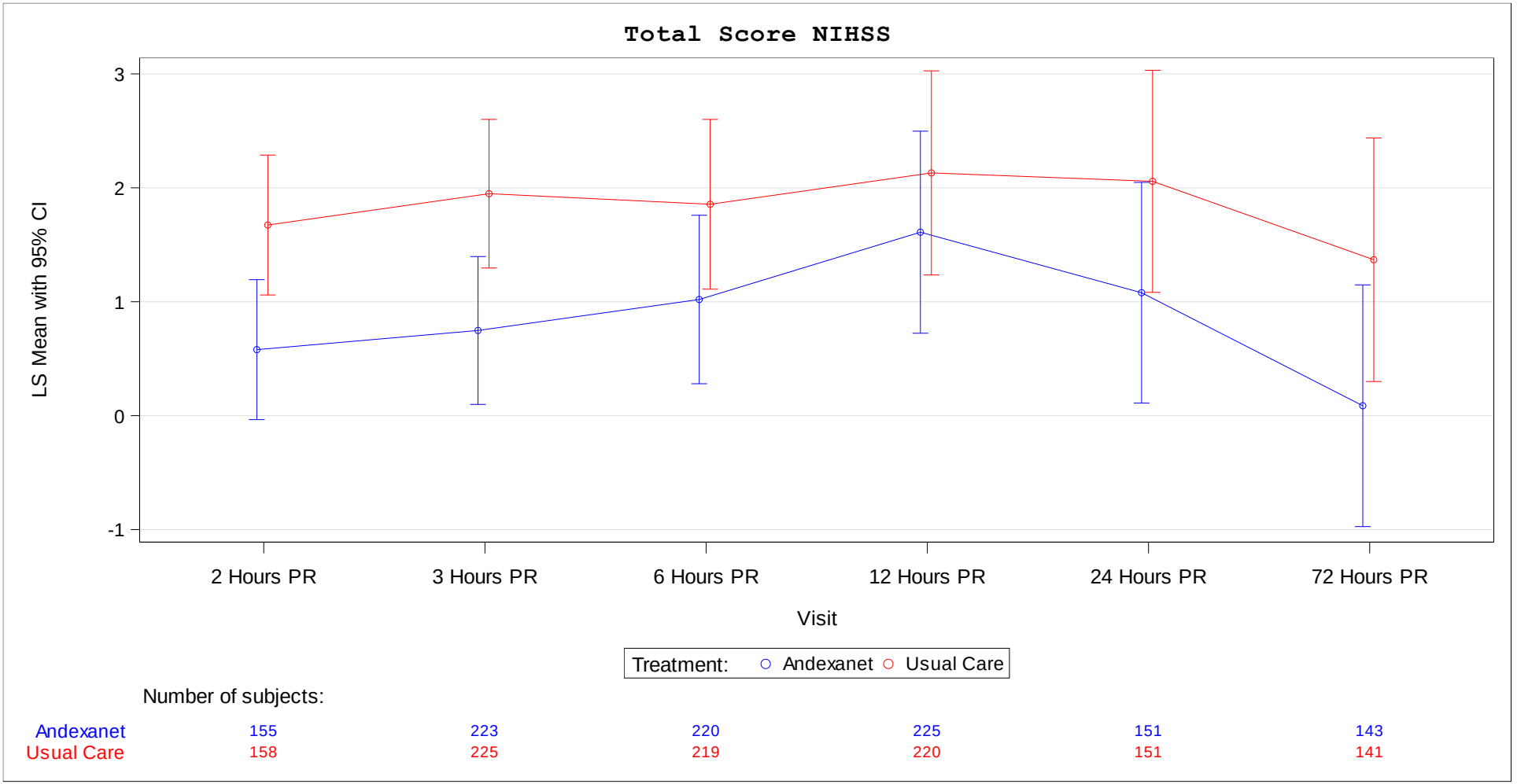
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.2
Summary of Mean Values and Change from Baseline for National Institutes of Health Stroke Scale (NIHSS) by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Total Score NIHSS	Baseline	239	10.8 (7.10)			231	10.0 (7.21)		
	2 Hours Post Randomization	155	12.3 (7.86)	155	0.6 (3.42)	158	12.0 (9.37)	158	1.9 (5.11)
	3 Hours Post Randomization	223	11.3 (8.10)	223	0.8 (3.75)	225	12.0 (9.70)	225	2.0 (5.85)
	6 Hours Post Randomization	220	11.8 (8.56)	220	1.0 (4.65)	219	11.7 (9.83)	219	1.8 (6.38)
	12 Hours Post Randomization	225	12.2 (9.29)	225	1.7 (6.00)	220	11.6 (9.85)	220	1.8 (7.25)
	24 Hours Post Randomization	151	12.4 (8.90)	151	0.9 (5.97)	151	11.6 (9.89)	151	1.9 (7.05)
	72 Hours Post Randomization	143	11.4 (8.89)	143	-0.1 (6.33)	141	10.3 (9.38)	141	0.9 (6.93)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation



CI: Confidence intervall, PR: Post Randomization

Table 2.5.4
MMRM Analysis of Change From Baseline in National Institutes of Health Stroke Scale (NIHSS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
Total Score NIHSS	2 Hours Post Randomization		0.58 (0.31)		1.67 (0.31)	-1.09 (-1.95, -0.24)	0.0126	-0.23 (-0.41, -0.05)
	3 Hours Post Randomization		0.75 (0.33)		1.95 (0.33)	-1.20 (-2.11, -0.29)	0.0099	-0.24 (-0.42, -0.06)
	6 Hours Post Randomization		1.02 (0.38)		1.86 (0.38)	-0.84 (-1.88, 0.21)	0.1156	-0.15 (-0.33, 0.04)
	12 Hours Post Randomization		1.61 (0.45)		2.13 (0.46)	-0.52 (-1.77, 0.73)	0.4151	-0.08 (-0.26, 0.11)
	24 Hours Post Randomization		1.08 (0.49)		2.06 (0.50)	-0.98 (-2.35, 0.39)	0.1606	-0.13 (-0.31, 0.05)
	72 Hours Post Randomization		0.09 (0.54)		1.37 (0.54)	-1.28 (-2.78, 0.22)	0.0939	-0.16 (-0.34, 0.03)
	Average Through Time	231	0.85 (0.35)	229	1.84 (0.35)	-0.98 (-1.95, -0.02)	0.0450	-0.19 (-0.37, -0.00)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.4.1
MMRM Analysis of Change From Baseline in National Institutes of Health Stroke Scale (NIHSS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Total Score NIHSS	Age												0.9221
	<65 years	13	6.8 (5.63)	11	0.28 (1.32)	14	10.0 (6.30)	14	1.09 (1.20)	-0.80 (-4.60, 2.99)	0.6588	-0.18 (-0.97, 0.62)	
	65 - 74 years	45	11.8 (7.65)	44	1.31 (1.07)	51	10.5 (8.02)	51	1.60 (1.06)	-0.29 (-3.20, 2.62)	0.8431	-0.04 (-0.44, 0.36)	
	>=75 years	181	10.8 (6.98)	176	0.87 (0.36)	166	9.9 (7.06)	164	1.79 (0.37)	-0.92 (-1.94, 0.10)	0.0780	-0.19 (-0.40, 0.02)	
	Sex												0.0449
	Male	128	10.6 (7.27)	124	1.02 (0.52)	116	10.8 (7.22)	115	2.97 (0.54)	-1.95 (-3.41, -0.50)	0.0087	-0.34 (-0.59, -0.08)	
	Female	111	10.9 (6.92)	107	0.69 (0.45)	115	9.2 (7.13)	114	0.70 (0.44)	-0.01 (-1.25, 1.23)	0.9873	-0.00 (-0.27, 0.26)	
	Race												0.2081
	White	216	10.5 (6.93)	209	0.96 (0.37)	212	9.6 (7.11)	210	1.79 (0.37)	-0.83 (-1.86, 0.20)	0.1136	-0.15 (-0.35, 0.04)	
	Other	15	11.8 (9.43)	14	-0.16 (1.44)	15	14.4 (7.68)	15	3.13 (1.22)	-3.29 (-7.23, 0.65)	0.0969	-0.63 (-1.38, 0.11)	
	Geographic Region 1												0.8576
	North America	29	8.7 (6.05)	27	0.65 (0.97)	26	9.9 (6.50)	25	1.83 (1.04)	-1.18 (-4.01, 1.65)	0.4057	-0.23 (-0.77, 0.32)	
	Europe	210	11.1 (7.19)	204	0.92 (0.37)	205	10.0 (7.31)	204	1.83 (0.38)	-0.91 (-1.95, 0.12)	0.0838	-0.17 (-0.36, 0.02)	
	Prior FXa Inhibitor												0.1349
	Apixaban	161	10.0 (6.60)	156	0.49 (0.43)	156	10.0 (7.21)	155	2.02 (0.43)	-1.54 (-2.72, -0.35)	0.0114	-0.29 (-0.51, -0.06)	
	Rivaroxaban	78	12.4 (7.80)	75	1.51 (0.62)	75	10.1 (7.27)	74	1.47 (0.64)	0.04 (-1.67, 1.74)	0.9653	0.01 (-0.31, 0.33)	
	Indication for prior FXa Inhibitor 1												0.8796
	Atrial Fibrillation/Flutter	207	10.8 (7.06)	200	0.86 (0.37)	194	9.9 (7.18)	192	1.92 (0.38)	-1.06 (-2.10, -0.02)	0.0462	-0.20 (-0.40, -0.00)	
	Venous Thromboembolism	19	11.4 (8.02)	18	0.97 (1.56)	30	10.3 (6.86)	30	1.79 (1.17)	-0.82 (-4.65, 3.01)	0.6680	-0.12 (-0.71, 0.46)	
	Other	13	9.0 (6.47)	13	1.16 (1.25)	7	11.4 (10.11)	7	1.19 (1.54)	-0.03 (-4.32, 4.26)	0.9875	-0.01 (-0.93, 0.91)	
	Indication for prior FXa Inhibitor 2												0.7581
	Atrial Fibrillation/Flutter	207	10.8 (7.06)	200	0.86 (0.37)	194	9.9 (7.18)	192	1.92 (0.38)	-1.06 (-2.10, -0.02)	0.0462	-0.20 (-0.40, -0.00)	
	Other	32	10.4 (7.41)	31	0.94 (1.03)	37	10.5 (7.43)	37	1.55 (0.93)	-0.61 (-3.34, 2.12)	0.6586	-0.11 (-0.58, 0.37)	
	Baseline Anti-FXa Activity 1												0.1326
	<30 ng/mL	15	13.0 (6.98)	15	1.24 (1.15)	11	11.5 (5.87)	11	-0.11 (1.31)	1.35 (-2.24, 4.95)	0.4428	0.30 (-0.49, 1.08)	
	>=30 ng/mL	209	10.8 (7.10)	203	0.63 (0.37)	201	10.0 (7.34)	199	2.00 (0.38)	-1.37 (-2.40, -0.33)	0.0097	-0.26 (-0.45, -0.06)	
	Baseline Anti-FXa Activity 2												0.3760
	<75 ng/mL	66	12.0 (7.02)	66	0.30 (0.73)	51	10.6 (6.56)	50	2.29 (0.84)	-1.99 (-4.19, 0.20)	0.0746	-0.33 (-0.70, 0.04)	
	>=75 ng/mL	158	10.5 (7.11)	152	0.84 (0.41)	161	9.9 (7.49)	160	1.73 (0.40)	-0.89 (-2.00, 0.22)	0.1150	-0.18 (-0.40, 0.05)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.4.1
MMRM Analysis of Change From Baseline in National Institutes of Health Stroke Scale (NIHSS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Total Score NIHSS	ICH Score at baseline												0.1867
	< 3	201	10.1 (6.82)	197	0.81 (0.36)	202	9.2 (6.78)	201	1.55 (0.36)	-0.73 (-1.73, 0.27)	0.1503	-0.14 (-0.34, 0.05)	
	>= 3	38	14.5 (7.43)	34	0.99 (1.11)	29	15.5 (7.83)	28	3.99 (1.22)	-3.00 (-6.29, 0.30)	0.0735	-0.46 (-0.97, 0.05)	
	Baseline Volume of Hematoma 1												0.2822
	<30 mL	188	9.7 (6.53)	185	0.42 (0.36)	192	9.2 (6.93)	190	1.10 (0.35)	-0.68 (-1.66, 0.30)	0.1715	-0.14 (-0.34, 0.06)	
	>=30 mL	51	14.8 (7.70)	46	2.64 (0.86)	38	14.1 (7.36)	38	4.79 (0.95)	-2.15 (-4.69, 0.38)	0.0948	-0.36 (-0.80, 0.07)	
	Baseline Volume of Hematoma 2												0.8922
	<0.5 mL	7	2.7 (4.31)	6	-1.16 (1.25)	11	3.5 (2.70)	11	-0.41 (1.07)	-0.75 (-4.09, 2.59)	0.6332	-0.21 (-1.21, 0.79)	
	>=0.5 mL	232	11.0 (7.03)	225	0.91 (0.35)	219	10.3 (7.22)	217	1.88 (0.36)	-0.97 (-1.94, 0.01)	0.0517	-0.18 (-0.37, 0.00)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	214	11.7 (6.84)	207		217	10.3 (7.17)	216					
	Intracranial - intraventricular hemorrhage	2	5.0 (4.24)	2		1	10.0 (-)						
	Intracranial - subdural	13	3.8 (4.10)	13		5	0.8 (1.10)	5					
	Intracranial - subarachnoid	9	1.9 (3.59)	9		7	7.4 (7.70)	7					
	Time to Randomization since the last FXa Inhibitor Dose												0.1387
	<8 hours	100	10.9 (6.61)	95	1.14 (0.62)	102	9.8 (7.22)	102	3.01 (0.62)	-1.87 (-3.54, -0.20)	0.0287	-0.30 (-0.59, -0.02)	
	>=8 hours	132	10.3 (7.32)	130	0.62 (0.41)	129	10.2 (7.22)	127	0.97 (0.41)	-0.35 (-1.49, 0.79)	0.5435	-0.08 (-0.32, 0.17)	
	Intended Usual Care Agent												0.0585
	PCC	159	12.0 (7.07)	152	0.87 (0.43)	155	10.4 (7.07)	154	2.17 (0.43)	-1.30 (-2.49, -0.11)	0.0324	-0.24 (-0.47, -0.02)	
	Other	18	10.4 (6.68)	18	1.04 (0.69)	11	5.6 (5.77)	11	-0.06 (0.88)	1.10 (-1.20, 3.39)	0.3340	0.36 (-0.39, 1.12)	
	Unknown	62	7.6 (6.32)	61	NE	65	9.7 (7.58)	64	NE	NE		NE	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.5
Proportion of Participants with NIHSS score increase >=7 at 12 hours post-randomization (NRI)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	30/241 (12.4)	32/233 (13.7)
Number of missing values	0	0
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.91 (0.57, 1.45)	
p-value	0.6933	
Odds Ratio (95% CI)	0.90 (0.53, 1.53)	
p-value	0.6933	
Risk Difference (95% CI)	-1.22 (-7.27, 4.84)	
p-value	0.6933	
p-value of CMH-Test	0.6938	
p-value of Breslow-Day Test	0.9299	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.5.5.1
Proportion of Participants with NIHSS score increase >=7 at 12 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					0.9010
<65 years	1/ 13 (7.7)	1/ 16 (6.3)	1.57 (0.12, 21.26)	0.7338	
65 - 74 years	7/ 45 (15.6)	10/ 51 (19.6)	0.84 (0.35, 2.02)	0.6949	
>=75 years	22/ 183 (12.0)	21/ 166 (12.7)	0.94 (0.54, 1.64)	0.8182	
Sex					0.2914
Male	17/ 130 (13.1)	21/ 118 (17.8)	0.74 (0.41, 1.33)	0.3084	
Female	13/ 111 (11.7)	11/ 115 (9.6)	1.23 (0.58, 2.61)	0.5878	
Race					0.4353
White	29/ 217 (13.4)	29/ 213 (13.6)	0.99 (0.61, 1.59)	0.9516	
Other	1/ 15 (6.7)	3/ 16 (18.8)	0.43 (0.06, 3.28)	0.4148	
Geographic Region 1					0.7815
North America	4/ 29 (13.8)	5/ 27 (18.5)	0.75 (0.17, 3.23)	0.6970	
Europe	26/ 212 (12.3)	27/ 206 (13.1)	0.93 (0.56, 1.54)	0.7797	
Prior FXa Inhibitor					0.4250
Apixaban	18/ 162 (11.1)	22/ 158 (13.9)	0.79 (0.44, 1.42)	0.4393	
Rivaroxaban	12/ 79 (15.2)	10/ 75 (13.3)	1.18 (0.54, 2.58)	0.6753	
Indication for prior FXa Inhibitor 1					0.6591
Atrial Fibrillation/Flutter	25/ 208 (12.0)	28/ 194 (14.4)	0.85 (0.51, 1.39)	0.5104	
Venous Thromboembolism	2/ 20 (10.0)	3/ 31 (9.7)	1.35 (0.25, 7.22)	0.7252	
Other	3/ 13 (23.1)	1/ 8 (12.5)	2.00 (0.24, 16.41)	0.5186	
Indication for prior FXa Inhibitor 2					0.3790
Atrial Fibrillation/Flutter	25/ 208 (12.0)	28/ 194 (14.4)	0.85 (0.51, 1.39)	0.5104	
Other	5/ 33 (15.2)	4/ 39 (10.3)	1.54 (0.45, 5.27)	0.4950	
Baseline Anti-FXa Activity 1					0.2069
<30 ng/mL	3/ 15 (20.0)	0/ 11 (0.0)	3.03 (0.38, 24.12)	0.2950	
>=30 ng/mL	24/ 211 (11.4)	30/ 202 (14.9)	0.77 (0.47, 1.26)	0.2969	
Baseline Anti-FXa Activity 2					0.8293
<75 ng/mL	8/ 67 (11.9)	8/ 52 (15.4)	0.78 (0.31, 1.94)	0.5871	
>=75 ng/mL	19/ 159 (11.9)	22/ 161 (13.7)	0.87 (0.49, 1.55)	0.6427	
ICH Score at baseline					0.3200
< 3	23/ 203 (11.3)	23/ 204 (11.3)	1.00 (0.58, 1.72)	0.9905	
>= 3	7/ 38 (18.4)	9/ 29 (31.0)	0.60 (0.25, 1.42)	0.2437	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 2.5.5.1
Proportion of Participants with NIHSS score increase >=7 at 12 hours post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.6068
<30 mL	18/ 190 (9.5)	19/ 193 (9.8)	0.97 (0.53, 1.79)	0.9328	
>=30 mL	12/ 51 (23.5)	12/ 39 (30.8)	0.77 (0.38, 1.52)	0.4458	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 7 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	30/ 234 (12.8)	31/ 221 (14.0)	0.91 (0.57, 1.46)	0.7039	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	29/ 215 (13.5)	31/ 218 (14.2)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 13 (7.7)	0/ 5 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.8270
<8 hours	15/ 101 (14.9)	18/ 103 (17.5)	0.88 (0.47, 1.63)	0.6746	
>=8 hours	14/ 133 (10.5)	14/ 130 (10.8)	0.97 (0.48, 1.96)	0.9359	
Intended Usual Care Agent					0.9006
PCC	21/ 160 (13.1)	23/ 156 (14.7)	0.89 (0.51, 1.54)	0.6708	
Other	1/ 18 (5.6)	0/ 11 (0.0)	1.71 (0.08, 37.32)	0.7316	
Unknown	8/ 63 (12.7)	9/ 66 (13.6)	1.01 (0.41, 2.45)	0.9878	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.6.1
Completion Rates for Glasgow Coma Scale (GCS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) n/ N	Andexanet (N=241) Completion rate	Usual Care (N=233) n/ N	Usual Care (N=233) Completion rate
GCS01-Total Score	Baseline	240/ 241	99.59%	232/ 233	99.57%
	2 Hours Post Randomization	159/ 241	65.98%	158/ 233	67.81%
	3 Hours Post Randomization	156/ 241	64.73%	157/ 232	67.67%
	6 Hours Post Randomization	157/ 240	65.42%	153/ 232	65.95%
	12 Hours Post Randomization	156/ 239	65.27%	153/ 231	66.23%
	24 Hours Post Randomization	152/ 236	64.41%	151/ 226	66.81%
	72 Hours Post Randomization	144/ 228	63.16%	146/ 217	67.28%

n describes number of patients with non-missing value at the respective timepoint.
N defines number of patients still alive at beginning of visit window.

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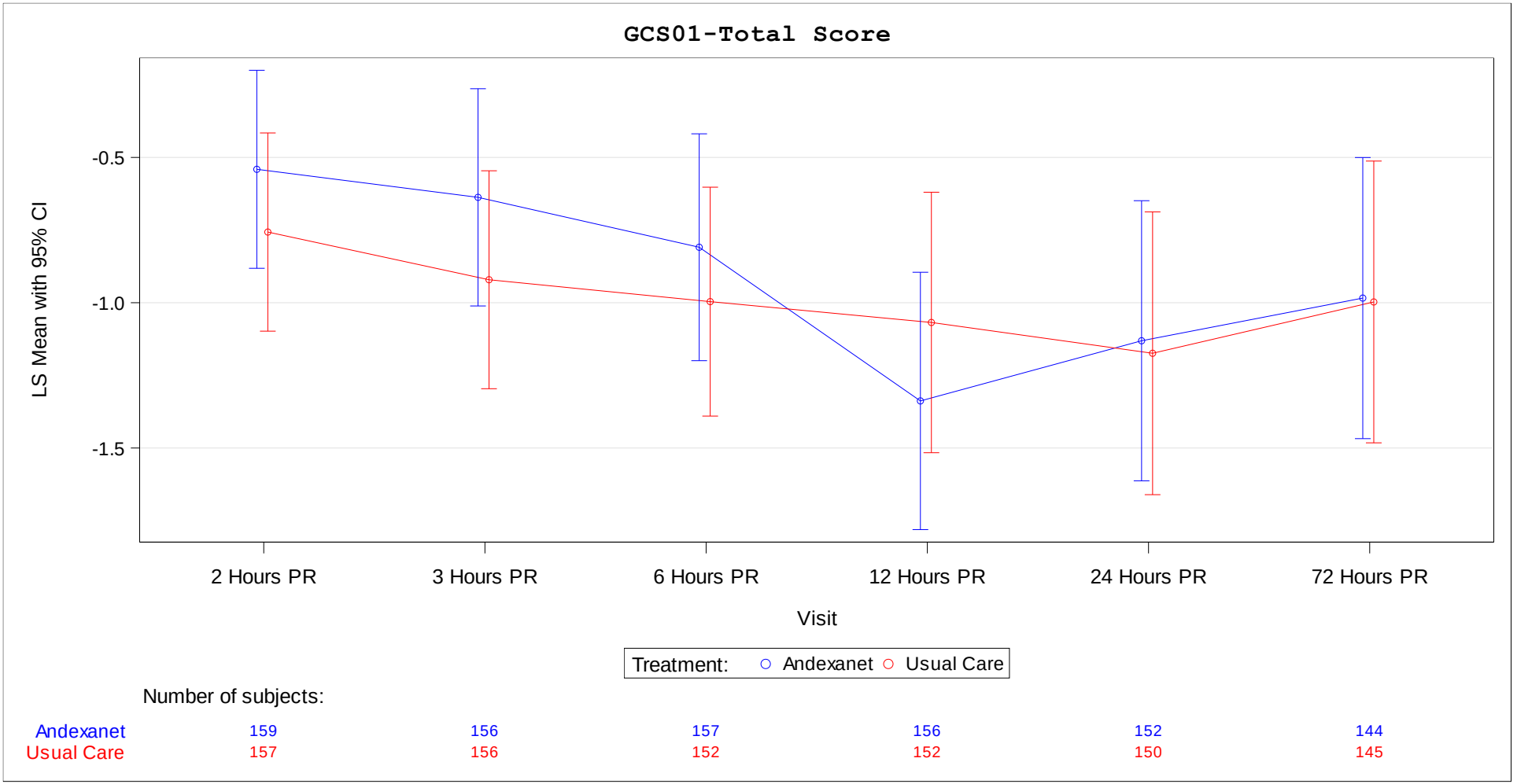
Table 2.6.2
Summary of Mean Values and Change from Baseline for Glasgow Coma Scale (GCS) by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
GCS01-Total Score	Baseline	240	13.8 (1.80)			232	13.6 (2.02)		
	2 Hours Post Randomization	159	13.1 (2.41)	159	-0.6 (1.90)	157	12.9 (3.21)	157	-0.8 (2.35)
	3 Hours Post Randomization	156	13.0 (2.60)	156	-0.7 (2.07)	156	12.8 (3.36)	156	-0.9 (2.64)
	6 Hours Post Randomization	157	12.9 (2.79)	157	-0.8 (2.19)	152	12.8 (3.32)	152	-0.9 (2.51)
	12 Hours Post Randomization	156	12.4 (3.23)	156	-1.3 (2.82)	152	12.8 (3.42)	152	-1.0 (2.65)
	24 Hours Post Randomization	152	12.8 (3.14)	152	-1.0 (2.72)	150	12.7 (3.62)	150	-1.0 (3.06)
	72 Hours Post Randomization	144	13.0 (3.19)	144	-0.9 (2.81)	145	13.1 (3.16)	145	-0.7 (2.81)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation



CI: Confidence intervall, PR: Post Randomization

Table 2.6.4
MMRM Analysis of Change From Baseline in Glasgow Coma Scale (GCS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) N	Andexanet (N=241) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
GCS01-Total Score	2 Hours Post Randomization		-0.54 (0.17)		-0.76 (0.17)	0.22 (-0.26, 0.69)	0.3698	0.10 (-0.12, 0.32)
	3 Hours Post Randomization		-0.64 (0.19)		-0.92 (0.19)	0.28 (-0.24, 0.80)	0.2852	0.12 (-0.10, 0.34)
	6 Hours Post Randomization		-0.81 (0.20)		-1.00 (0.20)	0.19 (-0.36, 0.73)	0.5011	0.07 (-0.14, 0.29)
	12 Hours Post Randomization		-1.34 (0.23)		-1.07 (0.23)	-0.27 (-0.89, 0.35)	0.3946	-0.09 (-0.31, 0.12)
	24 Hours Post Randomization		-1.13 (0.24)		-1.17 (0.25)	0.04 (-0.64, 0.72)	0.9008	0.01 (-0.20, 0.23)
	72 Hours Post Randomization		-0.98 (0.25)		-1.00 (0.25)	0.01 (-0.67, 0.69)	0.9691	0.00 (-0.21, 0.22)
	Average Through Time	164	-0.91 (0.18)	158	-0.99 (0.18)	0.08 (-0.42, 0.58)	0.7549	0.03 (-0.18, 0.25)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.6.4.1
MMRM Analysis of Change From Baseline in Glasgow Coma Scale (GCS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
GCS01-Total Score	Age												0.0749
	<65 years	13	14.2 (1.41)	8	0.11 (0.49)	15	14.1 (1.28)	11	-1.01 (0.43)	1.12 (-0.26, 2.49)	0.1042	0.75 (-0.20, 1.70)	
	65 - 74 years	44	14.1 (1.55)	31	-1.63 (0.52)	51	13.3 (2.29)	33	-0.60 (0.49)	-1.03 (-2.43, 0.36)	0.1424	-0.36 (-0.85, 0.14)	
	>=75 years	183	13.7 (1.88)	125	-0.82 (0.20)	166	13.7 (1.99)	114	-1.08 (0.21)	0.26 (-0.30, 0.81)	0.3641	0.12 (-0.14, 0.37)	
	Sex												0.1049
	Male	129	13.9 (1.70)	86	-0.92 (0.29)	117	13.6 (1.90)	87	-1.38 (0.28)	0.46 (-0.32, 1.24)	0.2477	0.17 (-0.13, 0.47)	
	Female	111	13.7 (1.92)	78	-0.92 (0.21)	115	13.6 (2.15)	71	-0.57 (0.22)	-0.35 (-0.94, 0.25)	0.2505	-0.19 (-0.51, 0.14)	
	Race												0.8229
	White	217	13.8 (1.85)	151	-0.89 (0.19)	212	13.6 (2.04)	145	-0.95 (0.19)	0.06 (-0.46, 0.58)	0.8175	0.03 (-0.20, 0.25)	
	Other	15	14.1 (1.41)	5	-1.82 (1.36)	16	13.2 (1.97)	10	-2.26 (0.95)	0.44 (-3.66, 4.55)	0.8013	0.14 (-0.94, 1.21)	
	Geographic Region 1												0.6016
	North America	29	14.2 (0.94)	18	-0.72 (0.50)	26	13.6 (2.04)	18	-1.16 (0.56)	0.44 (-1.02, 1.90)	0.5463	0.19 (-0.47, 0.84)	
	Europe	211	13.8 (1.89)	146	-0.93 (0.19)	206	13.6 (2.03)	140	-0.97 (0.19)	0.04 (-0.50, 0.57)	0.8914	0.02 (-0.22, 0.25)	
	Prior FXa Inhibitor												0.8602
	Apixaban	161	14.0 (1.63)	103	-0.80 (0.22)	157	13.5 (2.12)	105	-0.93 (0.22)	0.13 (-0.48, 0.74)	0.6747	0.06 (-0.21, 0.33)	
	Rivaroxaban	79	13.4 (2.07)	61	-1.05 (0.32)	75	13.9 (1.77)	53	-1.08 (0.34)	0.03 (-0.87, 0.93)	0.9415	0.01 (-0.35, 0.38)	
	Indication for prior FXa Inhibitor 1												0.4735
	Atrial Fibrillation/Flutter	207	13.9 (1.64)	139	-0.96 (0.20)	194	13.6 (2.04)	132	-1.09 (0.20)	0.13 (-0.42, 0.67)	0.6475	0.05 (-0.18, 0.29)	
	Venous Thromboembolism	20	12.9 (2.89)	18	-0.34 (0.62)	31	13.7 (1.80)	19	-0.57 (0.55)	0.23 (-1.42, 1.88)	0.7777	0.09 (-0.56, 0.73)	
	Other	13	13.8 (1.96)	7	-1.46 (0.78)	7	13.0 (2.77)	7	-0.24 (0.76)	-1.22 (-3.78, 1.33)	0.2967	-0.56 (-1.64, 0.51)	
	Indication for prior FXa Inhibitor 2												0.6783
	Atrial Fibrillation/Flutter	207	13.9 (1.64)	139	-0.96 (0.20)	194	13.6 (2.04)	132	-1.09 (0.20)	0.13 (-0.42, 0.67)	0.6475	0.05 (-0.18, 0.29)	
	Other	33	13.2 (2.57)	25	-0.65 (0.48)	38	13.6 (1.98)	26	-0.49 (0.44)	-0.16 (-1.46, 1.13)	0.8001	-0.07 (-0.62, 0.48)	
	Baseline Anti-FXa Activity 1												0.4225
	<30 ng/mL	15	13.4 (1.96)	13	-1.05 (0.51)	11	14.0 (1.26)	9	-0.54 (0.63)	-0.50 (-2.13, 1.12)	0.5252	-0.26 (-1.11, 0.59)	
	>=30 ng/mL	210	13.8 (1.80)	146	-0.85 (0.20)	202	13.6 (2.05)	142	-1.01 (0.20)	0.16 (-0.38, 0.69)	0.5626	0.07 (-0.16, 0.30)	
	Baseline Anti-FXa Activity 2												0.4083
	<75 ng/mL	67	13.5 (2.01)	53	-0.72 (0.36)	52	13.7 (1.63)	40	-1.20 (0.41)	0.48 (-0.59, 1.55)	0.3774	0.18 (-0.23, 0.59)	
	>=75 ng/mL	158	13.9 (1.70)	106	-0.96 (0.21)	161	13.6 (2.13)	111	-0.93 (0.21)	-0.03 (-0.60, 0.54)	0.9237	-0.01 (-0.28, 0.25)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.6.4.1
MMRM Analysis of Change From Baseline in Glasgow Coma Scale (GCS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Baseline Mean (SD)	Change from BL N	Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
GCS01-Total Score	ICH Score at baseline												0.4275
	< 3	202	14.1 (1.55)	138	-0.81 (0.18)	203	14.0 (1.66)	136	-0.78 (0.18)	-0.03 (-0.53, 0.47)	0.9147	-0.01 (-0.25, 0.22)	
	>= 3	38	12.3 (2.25)	26	-1.62 (0.61)	29	11.3 (2.74)	22	-2.32 (0.66)	0.70 (-1.09, 2.49)	0.4317	0.22 (-0.35, 0.79)	
	Baseline Volume of Hematoma 1												0.6818
	<30 mL	190	14.0 (1.63)	129	-0.52 (0.17)	193	13.9 (1.82)	128	-0.67 (0.17)	0.15 (-0.33, 0.62)	0.5405	0.08 (-0.17, 0.32)	
	>=30 mL	50	12.9 (2.16)	35	-2.50 (0.53)	38	12.6 (2.48)	29	-2.32 (0.57)	-0.18 (-1.70, 1.34)	0.8139	-0.06 (-0.55, 0.44)	
	Baseline Volume of Hematoma 2												NE
	<0.5 mL	7	14.4 (1.13)	4	NE	11	14.7 (0.65)	7	NE	NE		NE	
	>=0.5 mL	233	13.8 (1.82)	160	-0.94 (0.18)	220	13.6 (2.02)	150	-1.00 (0.19)	0.06 (-0.45, 0.57)	0.8197	0.03 (-0.20, 0.25)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	214	13.8 (1.77)	155		217	13.6 (2.00)	153					
	Intracranial - intraventricular hemorrhage	2	14.5 (0.71)	1		1	11.0 (-)						
	Intracranial - subdural	13	14.3 (1.65)	4		5	15.0 (0.00)	2					
	Intracranial - subarachnoid	10	13.6 (2.80)	4		8	13.1 (2.03)	2					
	Time to Randomization since the last FXa Inhibitor Dose												0.2361
	<8 hours	101	13.7 (1.97)	71	-0.84 (0.32)	102	13.7 (1.91)	77	-1.28 (0.31)	0.44 (-0.40, 1.28)	0.3056	0.16 (-0.16, 0.48)	
	>=8 hours	132	14.0 (1.60)	87	-0.82 (0.21)	130	13.5 (2.11)	81	-0.64 (0.21)	-0.17 (-0.75, 0.40)	0.5529	-0.09 (-0.39, 0.21)	
	Intended Usual Care Agent												
	PCC	160	13.6 (1.86)	146		155	13.6 (1.95)	146					
	Other	18	13.8 (1.58)	18		11	15.0 (0.00)	11					
	Unknown	62	14.2 (1.67)			66	13.5 (2.28)	1					

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.7.1
Completion Rates for Modified Rankin Scale (mRS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241) n/ N	Andexanet (N=241) Completion rate	Usual Care (N=233) n/ N	Usual Care (N=233) Completion rate
MRS01-Modified Rankin Scale Score	Baseline	233/ 241	96.68%	227/ 233	97.42%
	Day 30 Post Randomization	225/ 241	93.36%	222/ 233	95.28%

n describes number of patients with non-missing value at the respective timepoint.
N defines number of patients still alive at beginning of visit window.

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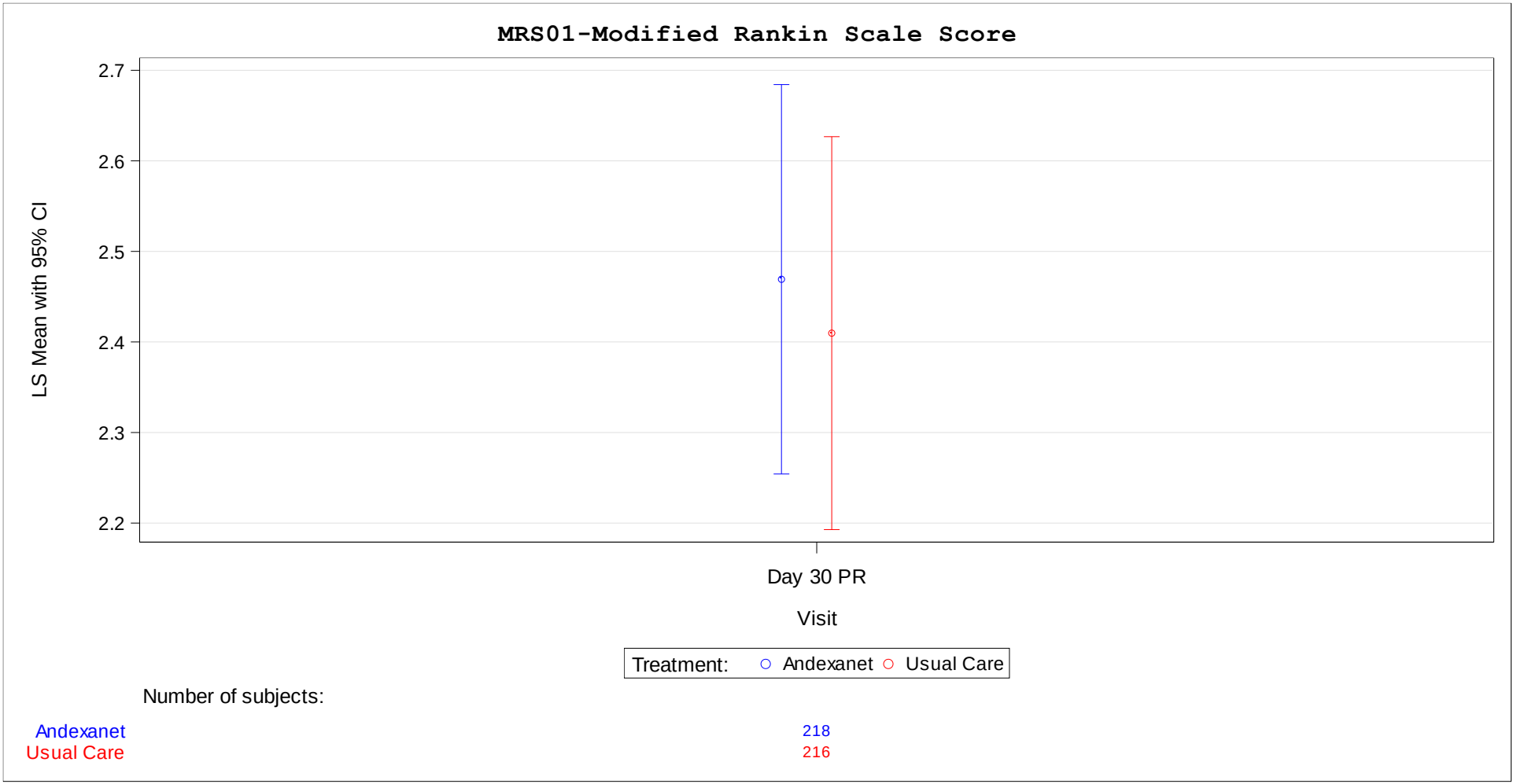
Table 2.7.2
Summary of Mean Values and Change from Baseline for Modified Rankin Scale (mRS) by Visit
Intent-To-Treat Set

		Andexanet (N=241)				Usual Care (N=233)			
		Value at Timepoint		Change from Baseline		Value at Timepoint		Change from Baseline	
Parameter	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
MRS01-Modified Rankin Scale Score	Baseline	233	1.7 (1.66)			227	1.6 (1.63)		
	Day 30 Post Randomization	218	4.2 (1.66)	218	2.5 (2.08)	217	4.1 (1.74)	216	2.5 (1.86)

N represents number of patients with non-missing baseline and visit values.
SD: Standard Deviation



CI: Confidence intervall, PR: Post Randomization

Table 2.7.4
MMRM Analysis of Change From Baseline in Modified Rankin Scale (mRS) by Visit
Intent-To-Treat Set

Parameter	Visit	Andexanet (N=241)		Usual Care (N=233)		Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)
		N	LSMean (SE)	N	LSMean (SE)			
MRS01-Modified Rankin Scale Score	Day 30 Post Randomization		2.47 (0.11)		2.41 (0.11)	0.06 (-0.24, 0.36)	0.6993	0.04 (-0.15, 0.22)
	Average Through Time	218	2.47 (0.11)	216	2.41 (0.11)	0.06 (-0.24, 0.36)	0.6993	0.04 (-0.15, 0.22)

Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.7.4.1
MMRM Analysis of Change From Baseline in Modified Rankin Scale (mRS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N Mean (SD)	Andexanet (N=241) Change from BL N LSMean (SE)	Usual Care (N=233) Baseline N Mean (SD)	Usual Care (N=233) Change from BL N LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
MRS01-Modified Rankin Scale Score	Age								0.9707
	<65 years	12 0.6 (1.24)	11 1.81 (0.58)	14 1.0 (1.36)	14 1.92 (0.53)	-0.11 (-1.70, 1.49)	0.8919	-0.05 (-0.84, 0.74)	
	65 - 74 years	42 1.8 (1.72)	38 2.47 (0.28)	49 1.0 (1.34)	47 2.42 (0.26)	0.05 (-0.71, 0.81)	0.8920	0.03 (-0.40, 0.46)	
	>=75 years	179 1.8 (1.65)	169 2.50 (0.12)	164 1.8 (1.69)	155 2.42 (0.12)	0.08 (-0.25, 0.42)	0.6317	0.05 (-0.17, 0.27)	
	Sex								0.0380
	Male	126 1.5 (1.59)	119 2.51 (0.15)	114 1.5 (1.59)	108 2.76 (0.16)	-0.26 (-0.69, 0.17)	0.2396	-0.15 (-0.41, 0.11)	
	Female	107 2.0 (1.69)	99 2.42 (0.15)	113 1.7 (1.68)	108 2.04 (0.15)	0.38 (-0.04, 0.80)	0.0796	0.24 (-0.03, 0.52)	
	Race								0.6437
	White	213 1.7 (1.63)	200 2.49 (0.11)	211 1.6 (1.64)	200 2.41 (0.12)	0.09 (-0.23, 0.40)	0.5971	0.05 (-0.14, 0.25)	
	Other	15 2.5 (1.96)	13 2.11 (0.43)	12 1.7 (1.87)	12 2.32 (0.44)	-0.21 (-1.51, 1.09)	0.7361	-0.13 (-0.92, 0.65)	
	Geographic Region 1								0.1504
	North America	29 1.6 (1.70)	28 1.97 (0.29)	25 1.8 (1.80)	24 2.51 (0.33)	-0.54 (-1.42, 0.34)	0.2264	-0.34 (-0.88, 0.21)	
	Europe	204 1.8 (1.65)	190 2.54 (0.12)	202 1.5 (1.61)	192 2.40 (0.12)	0.14 (-0.19, 0.46)	0.4076	0.08 (-0.12, 0.28)	
	Prior FXa Inhibitor								0.0149
	Apixaban	156 1.7 (1.72)	145 2.25 (0.13)	154 1.7 (1.67)	145 2.46 (0.13)	-0.21 (-0.57, 0.16)	0.2705	-0.13 (-0.36, 0.10)	
	Rivaroxaban	77 1.7 (1.54)	73 2.91 (0.20)	73 1.3 (1.53)	71 2.31 (0.20)	0.60 (0.06, 1.14)	0.0299	0.35 (0.02, 0.68)	
	Indication for prior FXa Inhibitor 1								0.6820
	Atrial Fibrillation/Flutter	201 1.7 (1.65)	189 2.56 (0.12)	190 1.5 (1.65)	179 2.49 (0.12)	0.07 (-0.26, 0.40)	0.6633	0.04 (-0.16, 0.25)	
	Venous Thromboembolism	19 1.8 (1.69)	17 2.54 (0.37)	30 1.9 (1.63)	30 2.19 (0.27)	0.35 (-0.54, 1.24)	0.4320	0.23 (-0.36, 0.83)	
	Other	13 2.2 (1.77)	12 1.22 (0.46)	7 1.3 (1.25)	7 1.63 (0.61)	-0.41 (-2.07, 1.26)	0.6085	-0.24 (-1.18, 0.69)	
	Indication for prior FXa Inhibitor 2								0.6392
	Atrial Fibrillation/Flutter	201 1.7 (1.65)	189 2.56 (0.12)	190 1.5 (1.65)	179 2.49 (0.12)	0.07 (-0.26, 0.40)	0.6633	0.04 (-0.16, 0.25)	
	Other	32 1.9 (1.70)	29 1.90 (0.29)	37 1.8 (1.57)	37 2.02 (0.26)	-0.12 (-0.89, 0.64)	0.7497	-0.08 (-0.56, 0.41)	
	Baseline Anti-FXa Activity 1								0.4178
	<30 ng/mL	15 1.7 (1.83)	15 2.88 (0.41)	11 2.0 (1.48)	11 2.39 (0.47)	0.49 (-0.78, 1.77)	0.4305	0.30 (-0.48, 1.08)	
	>=30 ng/mL	203 1.7 (1.64)	190 2.45 (0.12)	197 1.4 (1.60)	186 2.47 (0.12)	-0.02 (-0.36, 0.31)	0.8920	-0.01 (-0.22, 0.19)	
	Baseline Anti-FXa Activity 2								0.9121
	<75 ng/mL	65 1.7 (1.78)	60 2.79 (0.22)	50 1.2 (1.52)	49 2.75 (0.25)	0.05 (-0.61, 0.70)	0.8919	0.03 (-0.35, 0.40)	
	>=75 ng/mL	153 1.7 (1.60)	145 2.36 (0.13)	158 1.6 (1.62)	148 2.36 (0.13)	0.00 (-0.37, 0.37)	0.9866	0.00 (-0.23, 0.23)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

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Table 2.7.4.1
MMRM Analysis of Change From Baseline in Modified Rankin Scale (mRS) by Visit - Subgroup analysis
Intent-To-Treat Set

Parameter	Subgroup Level	Andexanet (N=241) Baseline N	Andexanet (N=241) Baseline Mean (SD)	Andexanet (N=241) Change from BL N	Andexanet (N=241) Change from BL LSMean (SE)	Usual Care (N=233) Baseline N	Usual Care (N=233) Baseline Mean (SD)	Usual Care (N=233) Change from BL N	Usual Care (N=233) Change from BL LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
MRS01-Modified Rankin Scale Score	ICH Score at baseline												0.1599
	< 3	196	1.7 (1.62)	183	2.38 (0.12)	198	1.5 (1.61)	188	2.28 (0.12)	0.10 (-0.23, 0.43)	0.5534	0.06 (-0.14, 0.26)	
	>= 3	37	1.9 (1.85)	35	2.91 (0.21)	29	1.9 (1.77)	28	3.33 (0.25)	-0.42 (-1.07, 0.24)	0.2072	-0.32 (-0.82, 0.18)	
	Baseline Volume of Hematoma 1												0.9604
	<30 mL	183	1.7 (1.65)	169	2.14 (0.12)	188	1.6 (1.63)	178	2.16 (0.12)	-0.01 (-0.35, 0.32)	0.9457	-0.01 (-0.22, 0.20)	
	>=30 mL	50	1.7 (1.69)	49	3.58 (0.14)	38	1.7 (1.68)	37	3.58 (0.16)	0.00 (-0.42, 0.43)	0.9927	0.00 (-0.42, 0.43)	
	Baseline Volume of Hematoma 2												0.3354
	<0.5 mL	7	2.0 (1.63)	6	1.21 (0.68)	11	1.2 (1.83)	11	0.40 (0.55)	0.80 (-0.99, 2.60)	0.3512	0.43 (-0.58, 1.44)	
	>=0.5 mL	226	1.7 (1.66)	212	2.50 (0.11)	215	1.6 (1.63)	204	2.51 (0.11)	-0.01 (-0.31, 0.29)	0.9461	-0.01 (-0.20, 0.19)	
	Index Bleeding Location 1												
	Intracranial - intracerebral hemorrhage	208	1.7 (1.65)	195		213	1.5 (1.59)	202					
	Intracranial - intraventricular hemorrhage	2	1.5 (2.12)	2		1	5.0 (-)	1					
	Intracranial - subdural	13	2.2 (1.88)	13		5	1.8 (2.05)	5					
	Intracranial - subarachnoid	9	1.6 (1.74)	8		7	2.7 (1.98)	7					
	Time to Randomization since the last FXa Inhibitor Dose												0.8215
	<8 hours	96	1.8 (1.70)	89	2.35 (0.17)	101	1.5 (1.57)	95	2.28 (0.17)	0.07 (-0.39, 0.54)	0.7489	0.05 (-0.24, 0.34)	
	>=8 hours	130	1.8 (1.63)	123	2.44 (0.15)	126	1.7 (1.69)	121	2.43 (0.15)	0.00 (-0.40, 0.41)	0.9814	0.00 (-0.25, 0.25)	
	Intended Usual Care Agent												0.0024
	PCC	154	1.4 (1.55)	144	3.00 (0.14)	152	1.2 (1.40)	146	2.72 (0.14)	0.28 (-0.09, 0.65)	0.1319	0.17 (-0.06, 0.40)	
	Other	18	1.6 (1.46)	17	3.09 (0.46)	11	0.7 (1.27)	9	2.00 (0.61)	1.08 (-0.46, 2.63)	0.1593	0.56 (-0.26, 1.39)	
	Unknown	61	2.6 (1.67)	57	0.97 (0.19)	64	2.6 (1.74)	61	1.70 (0.18)	-0.73 (-1.25, -0.21)	0.0066	-0.51 (-0.87, -0.14)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from MMRM for change from baseline; treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes), visit and treatment*visit as fixed effects, participants as the random effect; baseline value as the covariate; an unstructured covariance matrix is used.
N describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, MMRM = Mixed Model Repeated Measure.

Table 2.7.5
Proportion of Participants with mRS Improvement of 15% at 30 days post-randomization (NRI)
Intent-To-Treat Set

	Andexanet (N=241)	Usual Care (N=233)
Number of subjects with reponse, n/N (%)	3/241 (1.2)	1/233 (0.4)
Number of missing values	0	0
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	2.93 (0.30, 28.24)	
p-value	0.3516	
Odds Ratio (95% CI)	2.96 (0.30, 28.85)	
p-value	0.3501	
Risk Difference (95% CI)	0.82 (-0.81, 2.45)	
p-value	0.3232	
p-value of CMH-Test	0.3290	
p-value of Breslow-Day Test	0.5138	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.7.5.1
Proportion of Participants with mRS Improvement of 15% at 30 days post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Age					
<65 years	0/ 13 (0.0)	0/ 16 (0.0)			
65 - 74 years	1/ 45 (2.2)	1/ 51 (2.0)			
>=75 years	2/ 183 (1.1)	0/ 166 (0.0)			
Sex					
Male	2/ 130 (1.5)	0/ 118 (0.0)			
Female	1/ 111 (0.9)	1/ 115 (0.9)			
Race					
White	3/ 217 (1.4)	1/ 213 (0.5)			
Other	0/ 15 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	2/ 29 (6.9)	0/ 27 (0.0)			
Europe	1/ 212 (0.5)	1/ 206 (0.5)			
Prior FXa Inhibitor					
Apixaban	2/ 162 (1.2)	0/ 158 (0.0)			
Rivaroxaban	1/ 79 (1.3)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	2/ 208 (1.0)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 20 (0.0)	0/ 31 (0.0)			
Other	1/ 13 (7.7)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	2/ 208 (1.0)	1/ 194 (0.5)			
Other	1/ 33 (3.0)	0/ 39 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	3/ 211 (1.4)	1/ 202 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	0/ 52 (0.0)			
>=75 ng/mL	2/ 159 (1.3)	1/ 161 (0.6)			
ICH Score at baseline					
< 3	3/ 203 (1.5)	1/ 204 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 2.7.5.1
Proportion of Participants with mRS Improvement of 15% at 30 days post-randomization (NRI) - Subgroup analysis
Intent-To-Treat Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	3/ 190 (1.6)	1/ 193 (0.5)			
>=30 mL	0/ 51 (0.0)	0/ 39 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	1/ 7 (14.3)	0/ 11 (0.0)			
>=0.5 mL	2/ 234 (0.9)	1/ 221 (0.5)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	2/ 215 (0.9)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 13 (0.0)	0/ 5 (0.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 101 (1.0)	0/ 103 (0.0)			
>=8 hours	2/ 133 (1.5)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	0/ 160 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	3/ 63 (4.8)	1/ 66 (1.5)			

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
Analysis is stratified by time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.1
Proportion of Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	67/239 (28.0)	61/232 (26.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.07 (0.79, 1.43)	
p-value	0.6714	
Odds Ratio (95% CI)	1.09 (0.73, 1.64)	
p-value	0.6713	
Risk Difference (95% CI)	1.74 (-6.29, 9.77)	
p-value	0.6711	
p-value of CMH-Test	0.6716	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.1.1
Proportion of Deaths Through 30 Days Post-Randomization - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.7568
<65 years	1/ 11 (9.1)	2/ 17 (11.8)	0.77 (0.08, 7.54)	0.8244	
65 - 74 years	9/ 43 (20.9)	13/ 51 (25.5)	0.82 (0.39, 1.73)	0.6049	
>=75 years	57/ 185 (30.8)	46/ 164 (28.0)	1.10 (0.79, 1.52)	0.5731	
Sex					0.3710
Male	39/ 128 (30.5)	38/ 118 (32.2)	0.95 (0.65, 1.37)	0.7694	
Female	28/ 111 (25.2)	23/ 114 (20.2)	1.25 (0.77, 2.03)	0.3674	
Race					0.9273
White	62/ 216 (28.7)	57/ 212 (26.9)	1.07 (0.79, 1.45)	0.6750	
Other	3/ 14 (21.4)	3/ 16 (18.8)	1.14 (0.27, 4.78)	0.8548	
Geographic Region 1					0.4829
North America	7/ 27 (25.9)	9/ 28 (32.1)	0.81 (0.35, 1.86)	0.6136	
Europe	60/ 212 (28.3)	52/ 204 (25.5)	1.11 (0.81, 1.53)	0.5186	
Prior FXa Inhibitor					0.1377
Apixaban	39/ 162 (24.1)	42/ 157 (26.8)	0.90 (0.62, 1.31)	0.5831	
Rivaroxaban	28/ 77 (36.4)	19/ 75 (25.3)	1.44 (0.88, 2.34)	0.1467	
Indication for prior FXa Inhibitor 1					0.6068
Atrial Fibrillation/Flutter	60/ 205 (29.3)	55/ 194 (28.4)	1.03 (0.76, 1.41)	0.8397	
Venous Thromboembolism	6/ 21 (28.6)	5/ 30 (16.7)	1.71 (0.60, 4.89)	0.3133	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
Indication for prior FXa Inhibitor 2					0.6582
Atrial Fibrillation/Flutter	60/ 205 (29.3)	55/ 194 (28.4)	1.03 (0.76, 1.41)	0.8397	
Other	7/ 34 (20.6)	6/ 38 (15.8)	1.30 (0.49, 3.50)	0.5984	
Baseline Anti-FXa Activity 1					0.3499
<30 ng/mL	7/ 15 (46.7)	3/ 11 (27.3)	1.71 (0.57, 5.17)	0.3413	
>=30 ng/mL	56/ 211 (26.5)	54/ 201 (26.9)	0.99 (0.72, 1.36)	0.9405	
Baseline Anti-FXa Activity 2					0.5809
<75 ng/mL	21/ 67 (31.3)	18/ 52 (34.6)	0.91 (0.54, 1.52)	0.7055	
>=75 ng/mL	42/ 159 (26.4)	39/ 160 (24.4)	1.08 (0.74, 1.58)	0.6757	
ICH Score at baseline					0.1911
< 3	51/ 201 (25.4)	45/ 203 (22.2)	1.14 (0.81, 1.62)	0.4497	
>= 3	16/ 38 (42.1)	16/ 29 (55.2)	0.76 (0.46, 1.25)	0.2861	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 3.1.1
Proportion of Deaths Through 30 Days Post-Randomization - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.8477
<30 mL	39/ 189 (20.6)	39/ 191 (20.4)	1.01 (0.68, 1.50)	0.9584	
>=30 mL	28/ 50 (56.0)	21/ 40 (52.5)	1.07 (0.73, 1.57)	0.7417	
Baseline Volume of Hematoma 2					0.3081
<0.5 mL	1/ 6 (16.7)	0/ 11 (0.0)	5.14 (0.24, 109.89)	0.2945	
>=0.5 mL	66/ 233 (28.3)	60/ 220 (27.3)	1.04 (0.77, 1.40)	0.8026	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	60/ 213 (28.2)	56/ 218 (25.7)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	1/ 1 (100.0)			
Intracranial - subdural	4/ 14 (28.6)	2/ 4 (50.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	1/ 8 (12.5)			
Time to Randomization since the last FXa Inhibitor Dose					0.5668
<8 hours	31/ 102 (30.4)	27/ 102 (26.5)	1.15 (0.74, 1.78)	0.5354	
>=8 hours	33/ 131 (25.2)	34/ 130 (26.2)	0.96 (0.64, 1.46)	0.8587	
Intended Usual Care Agent					0.1493
PCC	48/ 158 (30.4)	42/ 156 (26.9)	1.13 (0.80, 1.60)	0.4989	
Other	7/ 18 (38.9)	1/ 11 (9.1)	4.28 (0.60, 30.26)	0.1454	
Unknown	12/ 63 (19.0)	18/ 65 (27.7)	0.69 (0.36, 1.31)	0.2540	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.2
Proportion of Cardiovascular Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	67/239 (28.0)	60/232 (25.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.08 (0.80, 1.46)	
p-value	0.5958	
Odds Ratio (95% CI)	1.12 (0.74, 1.68)	
p-value	0.5956	
Risk Difference (95% CI)	2.17 (-5.84, 10.18)	
p-value	0.5952	
p-value of CMH-Test	0.5959	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.3
Proportion of Non-Cardiovascular Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.32 (0.01, 7.90)	
p-value	0.4889	
Odds Ratio (95% CI)	0.32 (0.01, 7.95)	
p-value	0.4886	
Risk Difference (95% CI)	-0.43 (-1.27, 0.41)	
p-value	0.3163	
p-value of CMH-Test	0.3101	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.4
Proportion of In-Hospital Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	54/239 (22.6)	51/232 (22.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.03 (0.73, 1.44)	
p-value	0.8734	
Odds Ratio (95% CI)	1.04 (0.67, 1.60)	
p-value	0.8734	
Risk Difference (95% CI)	0.61 (-6.91, 8.13)	
p-value	0.8733	
p-value of CMH-Test	0.8735	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.5
Proportion of In-Hospital Cardiovascular Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	54/239 (22.6)	50/232 (21.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.05 (0.75, 1.47)	
p-value	0.7852	
Odds Ratio (95% CI)	1.06 (0.69, 1.64)	
p-value	0.7851	
Risk Difference (95% CI)	1.04 (-6.45, 8.53)	
p-value	0.7850	
p-value of CMH-Test	0.7853	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.6
Proportion of In-Hospital Non-Cardiovascular Deaths Through 30 Days Post-Randomization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.32 (0.01, 7.90)	
p-value	0.4889	
Odds Ratio (95% CI)	0.32 (0.01, 7.95)	
p-value	0.4886	
Risk Difference (95% CI)	-0.43 (-1.27, 0.41)	
p-value	0.3163	
p-value of CMH-Test	0.3101	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.7
Proportion of Bleeding Related Deaths
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	12/239 (5.0)	16/232 (6.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.73 (0.35, 1.51)	
p-value	0.3917	
Odds Ratio (95% CI)	0.71 (0.33, 1.54)	
p-value	0.3913	
Risk Difference (95% CI)	-1.88 (-6.15, 2.40)	
p-value	0.3901	
p-value of CMH-Test	0.3899	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.8
Proportion of Bleeding Related Cardiovascular Deaths
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	12/239 (5.0)	15/232 (6.5)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.78 (0.37, 1.62)	
p-value	0.5014	
Odds Ratio (95% CI)	0.76 (0.35, 1.67)	
p-value	0.5012	
Risk Difference (95% CI)	-1.44 (-5.65, 2.76)	
p-value	0.5007	
p-value of CMH-Test	0.5006	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 3.9
Proportion of Bleeding Related Non-Cardiovascular Deaths
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.32 (0.01, 7.90)	
p-value	0.4889	
Odds Ratio (95% CI)	0.32 (0.01, 7.95)	
p-value	0.4886	
Risk Difference (95% CI)	-0.43 (-1.27, 0.41)	
p-value	0.3163	
p-value of CMH-Test	0.3101	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.1
Proportion of Participants With Adverse Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	205/239 (85.8)	190/232 (81.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.05 (0.97, 1.13)	
p-value	0.2543	
Odds Ratio (95% CI)	1.33 (0.81, 2.18)	
p-value	0.2537	
Risk Difference (95% CI)	3.88 (-2.77, 10.52)	
p-value	0.2528	
p-value of CMH-Test	0.2533	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.1.1
Proportion of Participants With Adverse Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.8614
<65 years	7/ 11 (63.6)	12/ 17 (70.6)	0.90 (0.52, 1.55)	0.7077	
65 - 74 years	38/ 43 (88.4)	43/ 51 (84.3)	1.05 (0.89, 1.23)	0.5660	
>=75 years	160/ 185 (86.5)	135/ 164 (82.3)	1.05 (0.96, 1.15)	0.2871	
Sex					0.6748
Male	113/ 128 (88.3)	98/ 118 (83.1)	1.06 (0.96, 1.18)	0.2456	
Female	92/ 111 (82.9)	92/ 114 (80.7)	1.03 (0.91, 1.16)	0.6717	
Race					0.6345
White	188/ 216 (87.0)	174/ 212 (82.1)	1.06 (0.98, 1.15)	0.1570	
Other	10/ 14 (71.4)	12/ 16 (75.0)	0.95 (0.62, 1.47)	0.8263	
Geographic Region 1					0.7700
North America	23/ 27 (85.2)	22/ 28 (78.6)	1.08 (0.84, 1.39)	0.5252	
Europe	182/ 212 (85.8)	168/ 204 (82.4)	1.04 (0.96, 1.13)	0.3308	
Prior FXa Inhibitor					0.3717
Apixaban	136/ 162 (84.0)	129/ 157 (82.2)	1.02 (0.93, 1.13)	0.6712	
Rivaroxaban	69/ 77 (89.6)	61/ 75 (81.3)	1.10 (0.97, 1.26)	0.1515	
Indication for prior FXa Inhibitor 1					0.2121
Atrial Fibrillation/Flutter	177/ 205 (86.3)	161/ 194 (83.0)	1.04 (0.96, 1.13)	0.3544	
Venous Thromboembolism	19/ 21 (90.5)	22/ 30 (73.3)	1.23 (0.95, 1.59)	0.1085	
Other	9/ 13 (69.2)	7/ 8 (87.5)	0.79 (0.51, 1.24)	0.3046	
Indication for prior FXa Inhibitor 2					0.7747
Atrial Fibrillation/Flutter	177/ 205 (86.3)	161/ 194 (83.0)	1.04 (0.96, 1.13)	0.3544	
Other	28/ 34 (82.4)	29/ 38 (76.3)	1.08 (0.85, 1.37)	0.5268	
Baseline Anti-FXa Activity 1					0.8847
<30 ng/mL	14/ 15 (93.3)	10/ 11 (90.9)	1.03 (0.82, 1.29)	0.8231	
>=30 ng/mL	180/ 211 (85.3)	164/ 201 (81.6)	1.05 (0.96, 1.14)	0.3118	
Baseline Anti-FXa Activity 2					0.3830
<75 ng/mL	60/ 67 (89.6)	42/ 52 (80.8)	1.11 (0.95, 1.30)	0.1941	
>=75 ng/mL	134/ 159 (84.3)	132/ 160 (82.5)	1.02 (0.93, 1.13)	0.6699	
ICH Score at baseline					0.4510
< 3	170/ 201 (84.6)	163/ 203 (80.3)	1.05 (0.96, 1.15)	0.2588	
>= 3	35/ 38 (92.1)	27/ 29 (93.1)	0.99 (0.86, 1.13)	0.8765	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.1.1
Proportion of Participants With Adverse Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.7435
<30 mL	159/ 189 (84.1)	153/ 191 (80.1)	1.05 (0.96, 1.15)	0.3068	
>=30 mL	46/ 50 (92.0)	36/ 40 (90.0)	1.02 (0.90, 1.17)	0.7436	
Baseline Volume of Hematoma 2					0.6147
<0.5 mL	3/ 6 (50.0)	4/ 11 (36.4)	1.38 (0.45, 4.21)	0.5769	
>=0.5 mL	202/ 233 (86.7)	185/ 220 (84.1)	1.03 (0.96, 1.11)	0.4338	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	181/ 213 (85.0)	179/ 218 (82.1)			
Intracranial - intraventricular hemorrhage	2/ 2 (100.0)	1/ 1 (100.0)			
Intracranial - subdural	12/ 14 (85.7)	3/ 4 (75.0)			
Intracranial - subarachnoid	10/ 10 (100.0)	6/ 8 (75.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.8721
<8 hours	82/ 102 (80.4)	78/ 102 (76.5)	1.05 (0.91, 1.21)	0.4965	
>=8 hours	117/ 131 (89.3)	112/ 130 (86.2)	1.04 (0.95, 1.14)	0.4373	
Intended Usual Care Agent					0.0567
PCC	138/ 158 (87.3)	126/ 156 (80.8)	1.08 (0.98, 1.19)	0.1135	
Other	18/ 18 (100.0)	8/ 11 (72.7)	1.38 (0.96, 1.97)	0.0846	
Unknown	49/ 63 (77.8)	56/ 65 (86.2)	0.90 (0.77, 1.06)	0.2218	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.2
Proportion of Participants With Serious Adverse Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	111/239 (46.4)	86/232 (37.1)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.25 (1.01, 1.55)	
p-value	0.0408	
Odds Ratio (95% CI)	1.47 (1.02, 2.13)	
p-value	0.0395	
Risk Difference (95% CI)	9.37 (0.51, 18.24)	
p-value	0.0382	
p-value of CMH-Test	0.0394	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.1.2.1
Proportion of Participants With Serious Adverse Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.3420
<65 years	4/ 11 (36.4)	6/ 17 (35.3)	1.03 (0.37, 2.84)	0.9539	
65 - 74 years	15/ 43 (34.9)	20/ 51 (39.2)	0.89 (0.52, 1.51)	0.6666	
>=75 years	92/ 185 (49.7)	60/ 164 (36.6)	1.36 (1.06, 1.74)	0.0153	
Sex					0.7785
Male	67/ 128 (52.3)	51/ 118 (43.2)	1.21 (0.93, 1.58)	0.1562	
Female	44/ 111 (39.6)	35/ 114 (30.7)	1.29 (0.90, 1.85)	0.1628	
Race					0.8821
White	102/ 216 (47.2)	81/ 212 (38.2)	1.24 (0.99, 1.54)	0.0612	
Other	5/ 14 (35.7)	5/ 16 (31.3)	1.14 (0.42, 3.14)	0.7957	
Geographic Region 1					0.7331
North America	12/ 27 (44.4)	11/ 28 (39.3)	1.13 (0.61, 2.11)	0.6985	
Europe	99/ 212 (46.7)	75/ 204 (36.8)	1.27 (1.01, 1.60)	0.0419	
Prior FXa Inhibitor					0.8859
Apixaban	69/ 162 (42.6)	54/ 157 (34.4)	1.24 (0.94, 1.64)	0.1351	
Rivaroxaban	42/ 77 (54.5)	32/ 75 (42.7)	1.28 (0.92, 1.78)	0.1474	
Indication for prior FXa Inhibitor 1					0.9199
Atrial Fibrillation/Flutter	96/ 205 (46.8)	73/ 194 (37.6)	1.24 (0.99, 1.57)	0.0653	
Venous Thromboembolism	11/ 21 (52.4)	11/ 30 (36.7)	1.43 (0.77, 2.66)	0.2614	
Other	4/ 13 (30.8)	2/ 8 (25.0)	1.23 (0.29, 5.25)	0.7791	
Indication for prior FXa Inhibitor 2					0.9112
Atrial Fibrillation/Flutter	96/ 205 (46.8)	73/ 194 (37.6)	1.24 (0.99, 1.57)	0.0653	
Other	15/ 34 (44.1)	13/ 38 (34.2)	1.29 (0.72, 2.31)	0.3909	
Baseline Anti-FXa Activity 1					0.5811
<30 ng/mL	10/ 15 (66.7)	7/ 11 (63.6)	1.05 (0.59, 1.86)	0.8734	
>=30 ng/mL	93/ 211 (44.1)	71/ 201 (35.3)	1.25 (0.98, 1.59)	0.0718	
Baseline Anti-FXa Activity 2					0.4648
<75 ng/mL	36/ 67 (53.7)	20/ 52 (38.5)	1.40 (0.93, 2.10)	0.1094	
>=75 ng/mL	67/ 159 (42.1)	58/ 160 (36.3)	1.16 (0.88, 1.53)	0.2826	
ICH Score at baseline					0.2555
< 3	89/ 201 (44.3)	69/ 203 (34.0)	1.30 (1.02, 1.67)	0.0356	
>= 3	22/ 38 (57.9)	17/ 29 (58.6)	0.99 (0.66, 1.49)	0.9523	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.2.1
Proportion of Participants With Serious Adverse Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9193
<30 mL	79/ 189 (41.8)	64/ 191 (33.5)	1.25 (0.96, 1.62)	0.0971	
>=30 mL	32/ 50 (64.0)	21/ 40 (52.5)	1.22 (0.85, 1.75)	0.2818	
Baseline Volume of Hematoma 2					0.6526
<0.5 mL	2/ 6 (33.3)	2/ 11 (18.2)	1.83 (0.34, 9.92)	0.4818	
>=0.5 mL	109/ 233 (46.8)	83/ 220 (37.7)	1.24 (1.00, 1.54)	0.0533	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	100/ 213 (46.9)	79/ 218 (36.2)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	1/ 1 (100.0)			
Intracranial - subdural	5/ 14 (35.7)	3/ 4 (75.0)			
Intracranial - subarachnoid	5/ 10 (50.0)	2/ 8 (25.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.2190
<8 hours	39/ 102 (38.2)	37/ 102 (36.3)	1.05 (0.74, 1.51)	0.7722	
>=8 hours	69/ 131 (52.7)	49/ 130 (37.7)	1.40 (1.06, 1.84)	0.0168	
Intended Usual Care Agent					0.0326
PCC	78/ 158 (49.4)	54/ 156 (34.6)	1.43 (1.09, 1.86)	0.0092	
Other	8/ 18 (44.4)	1/ 11 (9.1)	4.89 (0.70, 33.98)	0.1087	
Unknown	25/ 63 (39.7)	31/ 65 (47.7)	0.83 (0.56, 1.24)	0.3639	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.3
Proportion of Participants With Severe Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	101/239 (42.3)	82/232 (35.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.20 (0.95, 1.50)	
p-value	0.1255	
Odds Ratio (95% CI)	1.34 (0.92, 1.94)	
p-value	0.1241	
Risk Difference (95% CI)	6.91 (-1.86, 15.69)	
p-value	0.1226	
p-value of CMH-Test	0.1242	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.1.3.1
Proportion of Participants With Severe Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.1371
<65 years	2/ 11 (18.2)	4/ 17 (23.5)	0.77 (0.17, 3.53)	0.7393	
65 - 74 years	11/ 43 (25.6)	19/ 51 (37.3)	0.69 (0.37, 1.28)	0.2361	
>=75 years	88/ 185 (47.6)	59/ 164 (36.0)	1.32 (1.03, 1.70)	0.0312	
Sex					0.6624
Male	58/ 128 (45.3)	47/ 118 (39.8)	1.14 (0.85, 1.52)	0.3871	
Female	43/ 111 (38.7)	35/ 114 (30.7)	1.26 (0.88, 1.81)	0.2076	
Race					0.9449
White	93/ 216 (43.1)	77/ 212 (36.3)	1.19 (0.94, 1.50)	0.1562	
Other	5/ 14 (35.7)	5/ 16 (31.3)	1.14 (0.42, 3.14)	0.7957	
Geographic Region 1					0.4624
North America	10/ 27 (37.0)	11/ 28 (39.3)	0.94 (0.48, 1.85)	0.8639	
Europe	91/ 212 (42.9)	71/ 204 (34.8)	1.23 (0.97, 1.57)	0.0916	
Prior FXa Inhibitor					0.7288
Apixaban	61/ 162 (37.7)	51/ 157 (32.5)	1.16 (0.86, 1.57)	0.3349	
Rivaroxaban	40/ 77 (51.9)	31/ 75 (41.3)	1.26 (0.89, 1.77)	0.1938	
Indication for prior FXa Inhibitor 1					0.7397
Atrial Fibrillation/Flutter	90/ 205 (43.9)	70/ 194 (36.1)	1.22 (0.95, 1.55)	0.1135	
Venous Thromboembolism	9/ 21 (42.9)	10/ 30 (33.3)	1.29 (0.63, 2.61)	0.4861	
Other	2/ 13 (15.4)	2/ 8 (25.0)	0.62 (0.11, 3.54)	0.5868	
Indication for prior FXa Inhibitor 2					0.6384
Atrial Fibrillation/Flutter	90/ 205 (43.9)	70/ 194 (36.1)	1.22 (0.95, 1.55)	0.1135	
Other	11/ 34 (32.4)	12/ 38 (31.6)	1.02 (0.52, 2.01)	0.9439	
Baseline Anti-FXa Activity 1					0.5650
<30 ng/mL	8/ 15 (53.3)	6/ 11 (54.5)	0.98 (0.48, 2.00)	0.9511	
>=30 ng/mL	86/ 211 (40.8)	67/ 201 (33.3)	1.22 (0.95, 1.58)	0.1212	
Baseline Anti-FXa Activity 2					0.7588
<75 ng/mL	34/ 67 (50.7)	21/ 52 (40.4)	1.26 (0.84, 1.89)	0.2700	
>=75 ng/mL	60/ 159 (37.7)	52/ 160 (32.5)	1.16 (0.86, 1.57)	0.3284	
ICH Score at baseline					0.7374
< 3	78/ 201 (38.8)	66/ 203 (32.5)	1.19 (0.92, 1.55)	0.1881	
>= 3	23/ 38 (60.5)	16/ 29 (55.2)	1.10 (0.72, 1.66)	0.6630	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.3.1
Proportion of Participants With Severe Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.3866
<30 mL	73/ 189 (38.6)	59/ 191 (30.9)	1.25 (0.95, 1.65)	0.1152	
>=30 mL	28/ 50 (56.0)	22/ 40 (55.0)	1.02 (0.70, 1.48)	0.9245	
Baseline Volume of Hematoma 2					0.7396
<0.5 mL	1/ 6 (16.7)	1/ 11 (9.1)	1.83 (0.14, 24.37)	0.6461	
>=0.5 mL	100/ 233 (42.9)	80/ 220 (36.4)	1.18 (0.94, 1.48)	0.1562	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	92/ 213 (43.2)	74/ 218 (33.9)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	1/ 1 (100.0)			
Intracranial - subdural	5/ 14 (35.7)	3/ 4 (75.0)			
Intracranial - subarachnoid	3/ 10 (30.0)	3/ 8 (37.5)			
Time to Randomization since the last FXa Inhibitor Dose					0.7179
<8 hours	38/ 102 (37.3)	34/ 102 (33.3)	1.12 (0.77, 1.62)	0.5584	
>=8 hours	59/ 131 (45.0)	48/ 130 (36.9)	1.22 (0.91, 1.64)	0.1849	
Intended Usual Care Agent					0.0103
PCC	74/ 158 (46.8)	52/ 156 (33.3)	1.41 (1.06, 1.85)	0.0162	
Other	8/ 18 (44.4)	1/ 11 (9.1)	4.89 (0.70, 33.98)	0.1087	
Unknown	19/ 63 (30.2)	29/ 65 (44.6)	0.68 (0.43, 1.07)	0.0975	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.4
Proportion of Participants With Adverse Events leading to Discontinuation of Study Drug
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	NE	
p-value		
Odds Ratio (95% CI)	NE	
p-value		
Risk Difference (95% CI)	NE	
p-value		
p-value of CMH-Test	NE	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.4.1
Proportion of Participants With Adverse Events leading to Discontinuation of Study Drug - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.4.1
Proportion of Participants With Adverse Events leading to Discontinuation of Study Drug - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.5
Proportion of Participants With Adverse Events leading to Death
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	59/239 (24.7)	49/232 (21.1)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.17 (0.84, 1.63)	
p-value	0.3585	
Odds Ratio (95% CI)	1.22 (0.80, 1.88)	
p-value	0.3578	
Risk Difference (95% CI)	3.57 (-4.02, 11.15)	
p-value	0.3566	
p-value of CMH-Test	0.3579	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.5.1
Proportion of Participants With Adverse Events leading to Death - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.7526
<65 years	1/ 11 (9.1)	1/ 17 (5.9)	1.55 (0.11, 22.23)	0.7489	
65 - 74 years	8/ 43 (18.6)	11/ 51 (21.6)	0.86 (0.38, 1.95)	0.7223	
>=75 years	50/ 185 (27.0)	37/ 164 (22.6)	1.20 (0.83, 1.73)	0.3379	
Sex					0.9085
Male	37/ 128 (28.9)	29/ 118 (24.6)	1.18 (0.78, 1.78)	0.4454	
Female	22/ 111 (19.8)	20/ 114 (17.5)	1.13 (0.65, 1.95)	0.6616	
Race					0.3147
White	55/ 216 (25.5)	48/ 212 (22.6)	1.12 (0.80, 1.58)	0.4954	
Other	3/ 14 (21.4)	1/ 16 (6.3)	3.43 (0.40, 29.33)	0.2606	
Geographic Region 1					0.7799
North America	7/ 27 (25.9)	7/ 28 (25.0)	1.04 (0.42, 2.56)	0.9372	
Europe	52/ 212 (24.5)	42/ 204 (20.6)	1.19 (0.83, 1.70)	0.3381	
Prior FXa Inhibitor					0.3419
Apixaban	34/ 162 (21.0)	32/ 157 (20.4)	1.03 (0.67, 1.58)	0.8938	
Rivaroxaban	25/ 77 (32.5)	17/ 75 (22.7)	1.43 (0.85, 2.43)	0.1820	
Indication for prior FXa Inhibitor 1					0.6923
Atrial Fibrillation/Flutter	53/ 205 (25.9)	44/ 194 (22.7)	1.14 (0.80, 1.61)	0.4611	
Venous Thromboembolism	5/ 21 (23.8)	4/ 30 (13.3)	1.79 (0.54, 5.87)	0.3399	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
Indication for prior FXa Inhibitor 2					0.7811
Atrial Fibrillation/Flutter	53/ 205 (25.9)	44/ 194 (22.7)	1.14 (0.80, 1.61)	0.4611	
Other	6/ 34 (17.6)	5/ 38 (13.2)	1.34 (0.45, 4.00)	0.5986	
Baseline Anti-FXa Activity 1					0.6514
<30 ng/mL	6/ 15 (40.0)	3/ 11 (27.3)	1.47 (0.47, 4.62)	0.5128	
>=30 ng/mL	49/ 211 (23.2)	42/ 201 (20.9)	1.11 (0.77, 1.60)	0.5697	
Baseline Anti-FXa Activity 2					0.7793
<75 ng/mL	19/ 67 (28.4)	14/ 52 (26.9)	1.05 (0.59, 1.90)	0.8625	
>=75 ng/mL	36/ 159 (22.6)	31/ 160 (19.4)	1.17 (0.76, 1.79)	0.4747	
ICH Score at baseline					0.0922
< 3	47/ 201 (23.4)	36/ 203 (17.7)	1.32 (0.89, 1.94)	0.1623	
>= 3	12/ 38 (31.6)	13/ 29 (44.8)	0.70 (0.38, 1.31)	0.2666	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.5.1
Proportion of Participants With Adverse Events leading to Death - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9103
<30 mL	38/ 189 (20.1)	33/ 191 (17.3)	1.16 (0.76, 1.77)	0.4801	
>=30 mL	21/ 50 (42.0)	15/ 40 (37.5)	1.12 (0.67, 1.88)	0.6668	
Baseline Volume of Hematoma 2					0.3380
<0.5 mL	1/ 6 (16.7)	0/ 11 (0.0)	5.14 (0.24, 109.89)	0.2945	
>=0.5 mL	58/ 233 (24.9)	48/ 220 (21.8)	1.14 (0.82, 1.60)	0.4407	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	52/ 213 (24.4)	44/ 218 (20.2)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	1/ 1 (100.0)			
Intracranial - subdural	4/ 14 (28.6)	2/ 4 (50.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	1/ 8 (12.5)			
Time to Randomization since the last FXa Inhibitor Dose					0.8885
<8 hours	25/ 102 (24.5)	21/ 102 (20.6)	1.19 (0.71, 1.98)	0.5038	
>=8 hours	32/ 131 (24.4)	28/ 130 (21.5)	1.13 (0.73, 1.77)	0.5796	
Intended Usual Care Agent					0.1465
PCC	40/ 158 (25.3)	31/ 156 (19.9)	1.27 (0.84, 1.93)	0.2511	
Other	7/ 18 (38.9)	1/ 11 (9.1)	4.28 (0.60, 30.26)	0.1454	
Unknown	12/ 63 (19.0)	17/ 65 (26.2)	0.73 (0.38, 1.40)	0.3411	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Table 4.1.6
Proportion of Participants With Adjudicated Thrombotic Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	26/239 (10.9)	13/232 (5.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.94 (1.02, 3.68)	
p-value	0.0424	
Odds Ratio (95% CI)	2.06 (1.03, 4.11)	
p-value	0.0412	
Risk Difference (95% CI)	5.28 (0.34, 10.21)	
p-value	0.0361	
p-value of CMH-Test	0.0380	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.1.6.1
Proportion of Participants With Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.3221
<65 years	0/ 11 (0.0)	2/ 17 (11.8)	0.30 (0.02, 5.72)	0.4233	
65 - 74 years	5/ 43 (11.6)	4/ 51 (7.8)	1.48 (0.42, 5.18)	0.5372	
>=75 years	21/ 185 (11.4)	7/ 164 (4.3)	2.66 (1.16, 6.09)	0.0208	
Sex					0.1851
Male	13/ 128 (10.2)	9/ 118 (7.6)	1.33 (0.59, 3.00)	0.4895	
Female	13/ 111 (11.7)	4/ 114 (3.5)	3.34 (1.12, 9.93)	0.0302	
Race					0.5200
White	20/ 216 (9.3)	12/ 212 (5.7)	1.64 (0.82, 3.26)	0.1622	
Other	3/ 14 (21.4)	1/ 16 (6.3)	3.43 (0.40, 29.33)	0.2606	
Geographic Region 1					0.0580
North America	3/ 27 (11.1)	5/ 28 (17.9)	0.62 (0.16, 2.35)	0.4845	
Europe	23/ 212 (10.8)	8/ 204 (3.9)	2.77 (1.27, 6.04)	0.0107	
Prior FXa Inhibitor					0.4726
Apixaban	17/ 162 (10.5)	7/ 157 (4.5)	2.35 (1.00, 5.52)	0.0490	
Rivaroxaban	9/ 77 (11.7)	6/ 75 (8.0)	1.46 (0.55, 3.90)	0.4496	
Indication for prior FXa Inhibitor 1					0.4861
Atrial Fibrillation/Flutter	23/ 205 (11.2)	12/ 194 (6.2)	1.81 (0.93, 3.54)	0.0814	
Venous Thromboembolism	2/ 21 (9.5)	0/ 30 (0.0)	7.05 (0.36, 139.66)	0.2001	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
Indication for prior FXa Inhibitor 2					0.6028
Atrial Fibrillation/Flutter	23/ 205 (11.2)	12/ 194 (6.2)	1.81 (0.93, 3.54)	0.0814	
Other	3/ 34 (8.8)	1/ 38 (2.6)	3.35 (0.37, 30.73)	0.2845	
Baseline Anti-FXa Activity 1					0.1514
<30 ng/mL	1/ 15 (6.7)	2/ 11 (18.2)	0.37 (0.04, 3.55)	0.3865	
>=30 ng/mL	20/ 211 (9.5)	9/ 201 (4.5)	2.12 (0.99, 4.54)	0.0539	
Baseline Anti-FXa Activity 2					0.6107
<75 ng/mL	9/ 67 (13.4)	5/ 52 (9.6)	1.40 (0.50, 3.92)	0.5252	
>=75 ng/mL	12/ 159 (7.5)	6/ 160 (3.8)	2.01 (0.77, 5.23)	0.1512	
ICH Score at baseline					0.3035
< 3	24/ 201 (11.9)	11/ 203 (5.4)	2.20 (1.11, 4.38)	0.0241	
>= 3	2/ 38 (5.3)	2/ 29 (6.9)	0.76 (0.11, 5.10)	0.7803	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Table 4.1.6.1
Proportion of Participants With Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.6347
<30 mL	22/ 189 (11.6)	12/ 191 (6.3)	1.85 (0.94, 3.64)	0.0729	
>=30 mL	4/ 50 (8.0)	1/ 40 (2.5)	3.20 (0.37, 27.51)	0.2893	
Baseline Volume of Hematoma 2					0.2162
<0.5 mL	0/ 6 (0.0)	2/ 11 (18.2)	0.34 (0.02, 6.17)	0.4678	
>=0.5 mL	26/ 233 (11.2)	11/ 220 (5.0)	2.23 (1.13, 4.41)	0.0208	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	22/ 213 (10.3)	13/ 218 (6.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.7138
<8 hours	10/ 102 (9.8)	6/ 102 (5.9)	1.67 (0.63, 4.42)	0.3041	
>=8 hours	15/ 131 (11.5)	7/ 130 (5.4)	2.13 (0.90, 5.04)	0.0869	
Intended Usual Care Agent					0.7774
PCC	16/ 158 (10.1)	9/ 156 (5.8)	1.76 (0.80, 3.85)	0.1607	
Other	2/ 18 (11.1)	1/ 11 (9.1)	1.22 (0.12, 11.95)	0.8631	
Unknown	8/ 63 (12.7)	3/ 65 (4.6)	2.75 (0.76, 9.90)	0.1215	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Table 4.1.6.2
Summary of Anticoagulant Use Before or After the First Adjudicated Thrombotic Event
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
	n (%)	n (%)
Patients with no anticoagulants	57 (23.8)	64 (27.6)
Patients with no anticoagulants and any thrombotic events	2 (0.8)	1 (0.4)
Patients with no anticoagulants and no thrombotic events	55 (23.0)	63 (27.2)
Patients used any anticoagulants	182 (76.2)	168 (72.4)
Patients used any anticoagulants and with any thrombotic events	24 (10.0)	12 (5.2)
Patients used any anticoagulants before the first thrombotic event	9 (3.8)	8 (3.4)
Patients used any anticoagulants after the first thrombotic event	18 (7.5)	10 (4.3)
Patients used oral anticoagulants	26 (10.9)	22 (9.5)
Patients used oral anticoagulants and with any thrombotic events	4 (1.7)	3 (1.3)
Patients used oral anticoagulants before the first thrombotic event	1 (0.4)	0
Patients used oral anticoagulants after the first thrombotic event	3 (1.3)	3 (1.3)
Patients used parenteral anticoagulants	174 (72.8)	161 (69.4)
Patients used parenteral anticoagulants and with any thrombotic events	24 (10.0)	12 (5.2)
Patients used parenteral anticoagulants before the first thrombotic event	9 (3.8)	8 (3.4)
Patients used parenteral anticoagulants after the first thrombotic event	17 (7.1)	10 (4.3)

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Table 4.1.7
Proportion of Participants With Adjudicated Arterial Systemic Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	3/239 (1.3)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	2.91 (0.31, 27.79)	
p-value	0.3531	
Odds Ratio (95% CI)	2.94 (0.30, 28.44)	
p-value	0.3524	
Risk Difference (95% CI)	0.82 (-0.82, 2.47)	
p-value	0.3258	
p-value of CMH-Test	0.3303	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.7.1
Proportion of Participants With Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	1/ 43 (2.3)	1/ 51 (2.0)			
>=75 years	2/ 185 (1.1)	0/ 164 (0.0)			
Sex					
Male	1/ 128 (0.8)	0/ 118 (0.0)			
Female	2/ 111 (1.8)	1/ 114 (0.9)			
Race					
White	2/ 216 (0.9)	1/ 212 (0.5)			
Other	1/ 14 (7.1)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	3/ 212 (1.4)	1/ 204 (0.5)			
Prior FXa Inhibitor					
Apixaban	2/ 162 (1.2)	1/ 157 (0.6)			
Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	3/ 205 (1.5)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	3/ 205 (1.5)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)			
>=30 ng/mL	1/ 211 (0.5)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	2/ 67 (3.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	3/ 201 (1.5)	1/ 203 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.7.1
Proportion of Participants With Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	 p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	3/ 189 (1.6)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	3/ 233 (1.3)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	3/ 213 (1.4)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	2/ 102 (2.0)	1/ 102 (1.0)			
>=8 hours	1/ 131 (0.8)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	2/ 158 (1.3)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.8
Proportion of Participants With Adjudicated Deep Vein Thrombosis
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	2/232 (0.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.49 (0.04, 5.32)	
p-value	0.5539	
Odds Ratio (95% CI)	0.48 (0.04, 5.37)	
p-value	0.5537	
Risk Difference (95% CI)	-0.44 (-1.89, 1.00)	
p-value	0.5470	
p-value of CMH-Test	0.5455	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.8.1
Proportion of Participants With Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	1/ 51 (2.0)			
>=75 years	1/ 185 (0.5)	1/ 164 (0.6)			
Sex					
Male	1/ 128 (0.8)	2/ 118 (1.7)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	1/ 216 (0.5)	2/ 212 (0.9)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	2/ 28 (7.1)			
Europe	1/ 212 (0.5)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	1/ 157 (0.6)			
Rivaroxaban	0/ 77 (0.0)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	2/ 194 (1.0)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	2/ 194 (1.0)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	1/ 11 (9.1)			
>=30 ng/mL	1/ 211 (0.5)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	1/ 52 (1.9)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	2/ 203 (1.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.8.1
Proportion of Participants With Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	2/ 191 (1.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	1/ 233 (0.4)	2/ 220 (0.9)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	2/ 218 (0.9)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	1/ 102 (1.0)			
>=8 hours	0/ 131 (0.0)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	1/ 65 (1.5)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.9
Proportion of Participants With Adjudicated Ischemic Stroke
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	16/239 (6.7)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	5.18 (1.53, 17.53)	
p-value	0.0082	
Odds Ratio (95% CI)	5.48 (1.57, 19.06)	
p-value	0.0075	
Risk Difference (95% CI)	5.40 (1.92, 8.89)	
p-value	0.0024	
p-value of CMH-Test	0.0029	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.9.1
Proportion of Participants With Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.4945
<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
65 - 74 years	4/ 43 (9.3)	0/ 51 (0.0)	10.64 (0.59, 192.16)	0.1093	
>=75 years	12/ 185 (6.5)	3/ 164 (1.8)	3.55 (1.02, 12.35)	0.0467	
Sex					0.5236
Male	9/ 128 (7.0)	1/ 118 (0.8)	8.30 (1.07, 64.50)	0.0432	
Female	7/ 111 (6.3)	2/ 114 (1.8)	3.59 (0.76, 16.93)	0.1056	
Race					0.8227
White	12/ 216 (5.6)	3/ 212 (1.4)	3.93 (1.12, 13.71)	0.0321	
Other	2/ 14 (14.3)	0/ 16 (0.0)	5.67 (0.29, 108.91)	0.2501	
Geographic Region 1					0.9312
North America	2/ 27 (7.4)	0/ 28 (0.0)	5.18 (0.26, 103.15)	0.2813	
Europe	14/ 212 (6.6)	3/ 204 (1.5)	4.49 (1.31, 15.39)	0.0169	
Prior FXa Inhibitor					0.5744
Apixaban	13/ 162 (8.0)	2/ 157 (1.3)	6.30 (1.44, 27.46)	0.0143	
Rivaroxaban	3/ 77 (3.9)	1/ 75 (1.3)	2.92 (0.31, 27.47)	0.3483	
Indication for prior FXa Inhibitor 1					0.8869
Atrial Fibrillation/Flutter	14/ 205 (6.8)	3/ 194 (1.5)	4.42 (1.29, 15.13)	0.0181	
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
Indication for prior FXa Inhibitor 2					0.8884
Atrial Fibrillation/Flutter	14/ 205 (6.8)	3/ 194 (1.5)	4.42 (1.29, 15.13)	0.0181	
Other	2/ 34 (5.9)	0/ 38 (0.0)	5.57 (0.28, 112.12)	0.2621	
Baseline Anti-FXa Activity 1					0.7582
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
>=30 ng/mL	12/ 211 (5.7)	3/ 201 (1.5)	3.81 (1.09, 13.30)	0.0360	
Baseline Anti-FXa Activity 2					0.1904
<75 ng/mL	4/ 67 (6.0)	2/ 52 (3.8)	1.55 (0.30, 8.15)	0.6033	
>=75 ng/mL	9/ 159 (5.7)	1/ 160 (0.6)	9.06 (1.16, 70.65)	0.0355	
ICH Score at baseline					0.1463
< 3	15/ 201 (7.5)	2/ 203 (1.0)	7.57 (1.75, 32.70)	0.0067	
>= 3	1/ 38 (2.6)	1/ 29 (3.4)	0.76 (0.05, 11.69)	0.8461	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.9.1
Proportion of Participants With Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.8774
<30 mL	13/ 189 (6.9)	3/ 191 (1.6)	4.38 (1.27, 15.12)	0.0195	
>=30 mL	3/ 50 (6.0)	0/ 40 (0.0)	5.63 (0.30, 105.87)	0.2485	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	16/ 233 (6.9)	3/ 220 (1.4)	5.04 (1.49, 17.04)	0.0094	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	12/ 213 (5.6)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.3573
<8 hours	6/ 102 (5.9)	0/ 102 (0.0)	13.00 (0.74, 227.78)	0.0791	
>=8 hours	9/ 131 (6.9)	3/ 130 (2.3)	2.98 (0.82, 10.75)	0.0958	
Intended Usual Care Agent					0.4295
PCC	8/ 158 (5.1)	2/ 156 (1.3)	3.95 (0.85, 18.30)	0.0792	
Other	2/ 18 (11.1)	1/ 11 (9.1)	1.22 (0.12, 11.95)	0.8631	
Unknown	6/ 63 (9.5)	0/ 65 (0.0)	13.41 (0.77, 233.12)	0.0748	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.10
Proportion of Participants With Adjudicated Myocardial Infarction
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	11/239 (4.6)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	3.56 (1.01, 12.60)	
p-value	0.0490	
Odds Ratio (95% CI)	3.68 (1.01, 13.37)	
p-value	0.0476	
Risk Difference (95% CI)	3.31 (0.28, 6.34)	
p-value	0.0322	
p-value of CMH-Test	0.0347	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.10.1
Proportion of Participants With Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.1964
<65 years	0/ 11 (0.0)	1/ 17 (5.9)	0.50 (0.02, 11.28)	0.6629	
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)	NE		
>=75 years	11/ 185 (5.9)	2/ 164 (1.2)	4.88 (1.10, 21.67)	0.0374	
Sex					
Male	3/ 128 (2.3)	3/ 118 (2.5)			
Female	8/ 111 (7.2)	0/ 114 (0.0)			
Race					0.9335
White	9/ 216 (4.2)	3/ 212 (1.4)	2.94 (0.81, 10.73)	0.1016	
Other	1/ 14 (7.1)	0/ 16 (0.0)	3.40 (0.15, 77.34)	0.4427	
Geographic Region 1					0.0656
North America	1/ 27 (3.7)	2/ 28 (7.1)	0.52 (0.05, 5.39)	0.5825	
Europe	10/ 212 (4.7)	1/ 204 (0.5)	9.62 (1.24, 74.50)	0.0301	
Prior FXa Inhibitor					
Apixaban	7/ 162 (4.3)	2/ 157 (1.3)			
Rivaroxaban	4/ 77 (5.2)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					0.0684
Atrial Fibrillation/Flutter	11/ 205 (5.4)	2/ 194 (1.0)	5.20 (1.17, 23.18)	0.0304	
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
Other	0/ 13 (0.0)	1/ 8 (12.5)	0.21 (0.01, 4.71)	0.3284	
Indication for prior FXa Inhibitor 2					0.1396
Atrial Fibrillation/Flutter	11/ 205 (5.4)	2/ 194 (1.0)	5.20 (1.17, 23.18)	0.0304	
Other	0/ 34 (0.0)	1/ 38 (2.6)	0.37 (0.02, 8.82)	0.5400	
Baseline Anti-FXa Activity 1					NE
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)	NE		
>=30 ng/mL	8/ 211 (3.8)	2/ 201 (1.0)	3.81 (0.82, 17.73)	0.0881	
Baseline Anti-FXa Activity 2					
<75 ng/mL	5/ 67 (7.5)	1/ 52 (1.9)			
>=75 ng/mL	3/ 159 (1.9)	1/ 160 (0.6)			
ICH Score at baseline					0.4450
< 3	9/ 201 (4.5)	2/ 203 (1.0)	4.54 (0.99, 20.77)	0.0509	
>= 3	2/ 38 (5.3)	1/ 29 (3.4)	1.53 (0.15, 16.03)	0.7245	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.10.1
Proportion of Participants With Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.2479
<30 mL	10/ 189 (5.3)	2/ 191 (1.0)	5.05 (1.12, 22.75)	0.0349	
>=30 mL	1/ 50 (2.0)	1/ 40 (2.5)	0.80 (0.05, 12.40)	0.8732	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	11/ 233 (4.7)	3/ 220 (1.4)	3.46 (0.98, 12.24)	0.0540	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	10/ 213 (4.7)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 14 (7.1)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	4/ 102 (3.9)	2/ 102 (2.0)			
>=8 hours	7/ 131 (5.3)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	6/ 158 (3.8)	3/ 156 (1.9)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	5/ 63 (7.9)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.11
Proportion of Participants With Adjudicated Pulmonary Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	6/232 (2.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.16 (0.02, 1.33)	
p-value	0.0905	
Odds Ratio (95% CI)	0.16 (0.02, 1.32)	
p-value	0.0890	
Risk Difference (95% CI)	-2.17 (-4.37, 0.03)	
p-value	0.0535	
p-value of CMH-Test	0.0522	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.11.1
Proportion of Participants With Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	1/ 17 (5.9)			
65 - 74 years	1/ 43 (2.3)	3/ 51 (5.9)			
>=75 years	0/ 185 (0.0)	2/ 164 (1.2)			
Sex					
Male	1/ 128 (0.8)	5/ 118 (4.2)			
Female	0/ 111 (0.0)	1/ 114 (0.9)			
Race					
White	1/ 216 (0.5)	5/ 212 (2.4)			
Other	0/ 14 (0.0)	1/ 16 (6.3)			
Geographic Region 1					
North America	0/ 27 (0.0)	3/ 28 (10.7)			
Europe	1/ 212 (0.5)	3/ 204 (1.5)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	2/ 157 (1.3)			
Rivaroxaban	1/ 77 (1.3)	4/ 75 (5.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	6/ 194 (3.1)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	6/ 194 (3.1)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	2/ 11 (18.2)			
>=30 ng/mL	1/ 211 (0.5)	3/ 201 (1.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	2/ 52 (3.8)			
>=75 ng/mL	1/ 159 (0.6)	3/ 160 (1.9)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	6/ 203 (3.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.11.1
Proportion of Participants With Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	6/ 191 (3.1)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	1/ 233 (0.4)	5/ 220 (2.3)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	1/ 213 (0.5)	6/ 218 (2.8)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	3/ 102 (2.9)			
>=8 hours	0/ 131 (0.0)	3/ 130 (2.3)			
Intended Usual Care Agent					
PCC	1/ 158 (0.6)	3/ 156 (1.9)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	3/ 65 (4.6)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.12
Proportion of Participants With Adjudicated Transient Ischemic Attack
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	NE	
p-value		
Odds Ratio (95% CI)	NE	
p-value		
Risk Difference (95% CI)	NE	
p-value		
p-value of CMH-Test	NE	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.12.1
Proportion of Participants With Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.12.1
Proportion of Participants With Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.13
Proportion of Participants With Serious Adjudicated Thrombotic Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	24/239 (10.0)	12/232 (5.2)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.94 (0.99, 3.79)	
p-value	0.0519	
Odds Ratio (95% CI)	2.05 (1.00, 4.20)	
p-value	0.0506	
Risk Difference (95% CI)	4.87 (0.11, 9.63)	
p-value	0.0449	
p-value of CMH-Test	0.0470	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.13.1
Proportion of Participants With Serious Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.1531
<65 years	0/ 11 (0.0)	2/ 17 (11.8)	0.30 (0.02, 5.72)	0.4233	
65 - 74 years	3/ 43 (7.0)	4/ 51 (7.8)	0.89 (0.21, 3.76)	0.8735	
>=75 years	21/ 185 (11.4)	6/ 164 (3.7)	3.10 (1.28, 7.50)	0.0119	
Sex					0.2608
Male	12/ 128 (9.4)	8/ 118 (6.8)	1.38 (0.59, 3.26)	0.4595	
Female	12/ 111 (10.8)	4/ 114 (3.5)	3.08 (1.02, 9.27)	0.0452	
Race					0.8397
White	20/ 216 (9.3)	11/ 212 (5.2)	1.78 (0.88, 3.63)	0.1103	
Other	2/ 14 (14.3)	1/ 16 (6.3)	2.29 (0.23, 22.59)	0.4794	
Geographic Region 1					0.0750
North America	2/ 27 (7.4)	4/ 28 (14.3)	0.52 (0.10, 2.60)	0.4248	
Europe	22/ 212 (10.4)	8/ 204 (3.9)	2.65 (1.21, 5.81)	0.0152	
Prior FXa Inhibitor					0.4617
Apixaban	15/ 162 (9.3)	6/ 157 (3.8)	2.42 (0.96, 6.09)	0.0597	
Rivaroxaban	9/ 77 (11.7)	6/ 75 (8.0)	1.46 (0.55, 3.90)	0.4496	
Indication for prior FXa Inhibitor 1					0.4861
Atrial Fibrillation/Flutter	21/ 205 (10.2)	11/ 194 (5.7)	1.81 (0.89, 3.65)	0.0989	
Venous Thromboembolism	2/ 21 (9.5)	0/ 30 (0.0)	7.05 (0.36, 139.66)	0.2001	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
Indication for prior FXa Inhibitor 2					0.6020
Atrial Fibrillation/Flutter	21/ 205 (10.2)	11/ 194 (5.7)	1.81 (0.89, 3.65)	0.0989	
Other	3/ 34 (8.8)	1/ 38 (2.6)	3.35 (0.37, 30.73)	0.2845	
Baseline Anti-FXa Activity 1					0.1512
<30 ng/mL	1/ 15 (6.7)	2/ 11 (18.2)	0.37 (0.04, 3.55)	0.3865	
>=30 ng/mL	18/ 211 (8.5)	8/ 201 (4.0)	2.14 (0.95, 4.82)	0.0651	
Baseline Anti-FXa Activity 2					0.8215
<75 ng/mL	8/ 67 (11.9)	4/ 52 (7.7)	1.55 (0.49, 4.87)	0.4514	
>=75 ng/mL	11/ 159 (6.9)	6/ 160 (3.8)	1.84 (0.70, 4.87)	0.2160	
ICH Score at baseline					0.8228
< 3	22/ 201 (10.9)	11/ 203 (5.4)	2.02 (1.01, 4.06)	0.0480	
>= 3	2/ 38 (5.3)	1/ 29 (3.4)	1.53 (0.15, 16.03)	0.7245	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.13.1
Proportion of Participants With Serious Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.8545
<30 mL	21/ 189 (11.1)	11/ 191 (5.8)	1.93 (0.96, 3.89)	0.0662	
>=30 mL	3/ 50 (6.0)	1/ 40 (2.5)	2.40 (0.26, 22.20)	0.4405	
Baseline Volume of Hematoma 2					0.2137
<0.5 mL	0/ 6 (0.0)	2/ 11 (18.2)	0.34 (0.02, 6.17)	0.4678	
>=0.5 mL	24/ 233 (10.3)	10/ 220 (4.5)	2.27 (1.11, 4.63)	0.0248	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	20/ 213 (9.4)	12/ 218 (5.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.6314
<8 hours	10/ 102 (9.8)	6/ 102 (5.9)	1.67 (0.63, 4.42)	0.3041	
>=8 hours	14/ 131 (10.7)	6/ 130 (4.6)	2.32 (0.92, 5.84)	0.0752	
Intended Usual Care Agent					0.6012
PCC	15/ 158 (9.5)	8/ 156 (5.1)	1.85 (0.81, 4.24)	0.1454	
Other	1/ 18 (5.6)	1/ 11 (9.1)	0.61 (0.04, 8.81)	0.7176	
Unknown	8/ 63 (12.7)	3/ 65 (4.6)	2.75 (0.76, 9.90)	0.1215	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.14
Proportion of Participants With Serious Adjudicated Arterial Systemic Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	2/239 (0.8)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.94 (0.18, 21.27)	
p-value	0.5870	
Odds Ratio (95% CI)	1.95 (0.18, 21.65)	
p-value	0.5868	
Risk Difference (95% CI)	0.41 (-1.02, 1.84)	
p-value	0.5780	
p-value of CMH-Test	0.5804	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.14.1
Proportion of Participants With Serious Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	1/ 51 (2.0)			
>=75 years	2/ 185 (1.1)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	2/ 111 (1.8)	1/ 114 (0.9)			
Race					
White	1/ 216 (0.5)	1/ 212 (0.5)			
Other	1/ 14 (7.1)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	2/ 212 (0.9)	1/ 204 (0.5)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	1/ 157 (0.6)			
Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	2/ 205 (1.0)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	2/ 205 (1.0)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	1/ 211 (0.5)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	2/ 201 (1.0)	1/ 203 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.14.1
Proportion of Participants With Serious Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	2/ 189 (1.1)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	2/ 233 (0.9)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	2/ 213 (0.9)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	1/ 102 (1.0)			
>=8 hours	1/ 131 (0.8)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	1/ 158 (0.6)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.15
Proportion of Participants With Serious Adjudicated Deep Vein Thrombosis
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	2/232 (0.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.49 (0.04, 5.32)	
p-value	0.5539	
Odds Ratio (95% CI)	0.48 (0.04, 5.37)	
p-value	0.5537	
Risk Difference (95% CI)	-0.44 (-1.89, 1.00)	
p-value	0.5470	
p-value of CMH-Test	0.5455	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.15.1
Proportion of Participants With Serious Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	1/ 51 (2.0)			
>=75 years	1/ 185 (0.5)	1/ 164 (0.6)			
Sex					
Male	1/ 128 (0.8)	2/ 118 (1.7)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	1/ 216 (0.5)	2/ 212 (0.9)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	2/ 28 (7.1)			
Europe	1/ 212 (0.5)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	1/ 157 (0.6)			
Rivaroxaban	0/ 77 (0.0)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	2/ 194 (1.0)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	2/ 194 (1.0)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	1/ 11 (9.1)			
>=30 ng/mL	1/ 211 (0.5)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	1/ 52 (1.9)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	2/ 203 (1.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.15.1
Proportion of Participants With Serious Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	2/ 191 (1.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	1/ 233 (0.4)	2/ 220 (0.9)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	2/ 218 (0.9)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	1/ 102 (1.0)			
>=8 hours	0/ 131 (0.0)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	1/ 65 (1.5)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.16
Proportion of Participants With Serious Adjudicated Ischemic Stroke
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	14/239 (5.9)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	4.53 (1.32, 15.56)	
p-value	0.0164	
Odds Ratio (95% CI)	4.75 (1.35, 16.75)	
p-value	0.0154	
Risk Difference (95% CI)	4.56 (1.25, 7.88)	
p-value	0.0069	
p-value of CMH-Test	0.0080	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.16.1
Proportion of Participants With Serious Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.7587
<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
65 - 74 years	2/ 43 (4.7)	0/ 51 (0.0)	5.91 (0.29, 119.84)	0.2473	
>=75 years	12/ 185 (6.5)	3/ 164 (1.8)	3.55 (1.02, 12.35)	0.0467	
Sex					
Male	8/ 128 (6.3)	1/ 118 (0.8)			
Female	6/ 111 (5.4)	2/ 114 (1.8)			
Race					0.9332
White	12/ 216 (5.6)	3/ 212 (1.4)	3.93 (1.12, 13.71)	0.0321	
Other	1/ 14 (7.1)	0/ 16 (0.0)	3.40 (0.15, 77.34)	0.4427	
Geographic Region 1					0.8651
North America	1/ 27 (3.7)	0/ 28 (0.0)	3.11 (0.13, 73.11)	0.4817	
Europe	13/ 212 (6.1)	3/ 204 (1.5)	4.17 (1.21, 14.42)	0.0241	
Prior FXa Inhibitor					0.6616
Apixaban	11/ 162 (6.8)	2/ 157 (1.3)	5.33 (1.20, 23.66)	0.0278	
Rivaroxaban	3/ 77 (3.9)	1/ 75 (1.3)	2.92 (0.31, 27.47)	0.3483	
Indication for prior FXa Inhibitor 1					0.9178
Atrial Fibrillation/Flutter	12/ 205 (5.9)	3/ 194 (1.5)	3.79 (1.08, 13.21)	0.0368	
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
Indication for prior FXa Inhibitor 2					0.8158
Atrial Fibrillation/Flutter	12/ 205 (5.9)	3/ 194 (1.5)	3.79 (1.08, 13.21)	0.0368	
Other	2/ 34 (5.9)	0/ 38 (0.0)	5.57 (0.28, 112.12)	0.2621	
Baseline Anti-FXa Activity 1					0.8409
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
>=30 ng/mL	10/ 211 (4.7)	3/ 201 (1.5)	3.18 (0.89, 11.37)	0.0759	
Baseline Anti-FXa Activity 2					
<75 ng/mL	3/ 67 (4.5)	2/ 52 (3.8)			
>=75 ng/mL	8/ 159 (5.0)	1/ 160 (0.6)			
ICH Score at baseline					0.1740
< 3	13/ 201 (6.5)	2/ 203 (1.0)	6.56 (1.50, 28.72)	0.0125	
>= 3	1/ 38 (2.6)	1/ 29 (3.4)	0.76 (0.05, 11.69)	0.8461	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.16.1
Proportion of Participants With Serious Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9973
<30 mL	12/ 189 (6.3)	3/ 191 (1.6)	4.04 (1.16, 14.10)	0.0284	
>=30 mL	2/ 50 (4.0)	0/ 40 (0.0)	4.02 (0.20, 81.42)	0.3647	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	14/ 233 (6.0)	3/ 220 (1.4)	4.41 (1.28, 15.12)	0.0184	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	10/ 213 (4.7)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.3214
<8 hours	6/ 102 (5.9)	0/ 102 (0.0)	13.00 (0.74, 227.78)	0.0791	
>=8 hours	8/ 131 (6.1)	3/ 130 (2.3)	2.65 (0.72, 9.75)	0.1437	
Intended Usual Care Agent					
PCC	7/ 158 (4.4)	2/ 156 (1.3)			
Other	1/ 18 (5.6)	1/ 11 (9.1)			
Unknown	6/ 63 (9.5)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.17
Proportion of Participants With Serious Adjudicated Myocardial Infarction
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	11/239 (4.6)	2/232 (0.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	5.34 (1.20, 23.83)	
p-value	0.0282	
Odds Ratio (95% CI)	5.55 (1.22, 25.31)	
p-value	0.0269	
Risk Difference (95% CI)	3.74 (0.83, 6.65)	
p-value	0.0118	
p-value of CMH-Test	0.0133	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.17.1
Proportion of Participants With Serious Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.1178
<65 years	0/ 11 (0.0)	1/ 17 (5.9)	0.50 (0.02, 11.28)	0.6629	
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)	NE		
>=75 years	11/ 185 (5.9)	1/ 164 (0.6)	9.75 (1.27, 74.72)	0.0284	
Sex					
Male	3/ 128 (2.3)	2/ 118 (1.7)			
Female	8/ 111 (7.2)	0/ 114 (0.0)			
Race					0.8827
White	9/ 216 (4.2)	2/ 212 (0.9)	4.42 (0.97, 20.20)	0.0555	
Other	1/ 14 (7.1)	0/ 16 (0.0)	3.40 (0.15, 77.34)	0.4427	
Geographic Region 1					0.1997
North America	1/ 27 (3.7)	1/ 28 (3.6)	1.04 (0.07, 15.76)	0.9791	
Europe	10/ 212 (4.7)	1/ 204 (0.5)	9.62 (1.24, 74.50)	0.0301	
Prior FXa Inhibitor					
Apixaban	7/ 162 (4.3)	1/ 157 (0.6)			
Rivaroxaban	4/ 77 (5.2)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					0.0397
Atrial Fibrillation/Flutter	11/ 205 (5.4)	1/ 194 (0.5)	10.41 (1.36, 79.87)	0.0242	
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
Other	0/ 13 (0.0)	1/ 8 (12.5)	0.21 (0.01, 4.71)	0.3284	
Indication for prior FXa Inhibitor 2					0.0829
Atrial Fibrillation/Flutter	11/ 205 (5.4)	1/ 194 (0.5)	10.41 (1.36, 79.87)	0.0242	
Other	0/ 34 (0.0)	1/ 38 (2.6)	0.37 (0.02, 8.82)	0.5400	
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	8/ 211 (3.8)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	5/ 67 (7.5)	0/ 52 (0.0)			
>=75 ng/mL	3/ 159 (1.9)	1/ 160 (0.6)			
ICH Score at baseline					0.9225
< 3	9/ 201 (4.5)	2/ 203 (1.0)	4.54 (0.99, 20.77)	0.0509	
>= 3	2/ 38 (5.3)	0/ 29 (0.0)	3.85 (0.19, 77.16)	0.3786	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.17.1
Proportion of Participants With Serious Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.1461
<30 mL	10/ 189 (5.3)	1/ 191 (0.5)	10.11 (1.31, 78.17)	0.0267	
>=30 mL	1/ 50 (2.0)	1/ 40 (2.5)	0.80 (0.05, 12.40)	0.8732	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	11/ 233 (4.7)	2/ 220 (0.9)	5.19 (1.16, 23.17)	0.0308	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	10/ 213 (4.7)	2/ 218 (0.9)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 14 (7.1)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	4/ 102 (3.9)	2/ 102 (2.0)			
>=8 hours	7/ 131 (5.3)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	6/ 158 (3.8)	2/ 156 (1.3)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	5/ 63 (7.9)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.18
Proportion of Participants With Serious Adjudicated Pulmonary Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	6/232 (2.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.16 (0.02, 1.33)	
p-value	0.0905	
Odds Ratio (95% CI)	0.16 (0.02, 1.32)	
p-value	0.0890	
Risk Difference (95% CI)	-2.17 (-4.37, 0.03)	
p-value	0.0535	
p-value of CMH-Test	0.0522	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.18.1
Proportion of Participants With Serious Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	1/ 17 (5.9)			
65 - 74 years	1/ 43 (2.3)	3/ 51 (5.9)			
>=75 years	0/ 185 (0.0)	2/ 164 (1.2)			
Sex					
Male	1/ 128 (0.8)	5/ 118 (4.2)			
Female	0/ 111 (0.0)	1/ 114 (0.9)			
Race					
White	1/ 216 (0.5)	5/ 212 (2.4)			
Other	0/ 14 (0.0)	1/ 16 (6.3)			
Geographic Region 1					
North America	0/ 27 (0.0)	3/ 28 (10.7)			
Europe	1/ 212 (0.5)	3/ 204 (1.5)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	2/ 157 (1.3)			
Rivaroxaban	1/ 77 (1.3)	4/ 75 (5.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	6/ 194 (3.1)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	6/ 194 (3.1)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	2/ 11 (18.2)			
>=30 ng/mL	1/ 211 (0.5)	3/ 201 (1.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	2/ 52 (3.8)			
>=75 ng/mL	1/ 159 (0.6)	3/ 160 (1.9)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	6/ 203 (3.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.18.1
Proportion of Participants With Serious Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	 p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	6/ 191 (3.1)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	1/ 233 (0.4)	5/ 220 (2.3)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	1/ 213 (0.5)	6/ 218 (2.8)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	3/ 102 (2.9)			
>=8 hours	0/ 131 (0.0)	3/ 130 (2.3)			
Intended Usual Care Agent					
PCC	1/ 158 (0.6)	3/ 156 (1.9)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	3/ 65 (4.6)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.19
Proportion of Participants With Serious Adjudicated Transient Ischemic Attack
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	NE	
p-value		
Odds Ratio (95% CI)	NE	
p-value		
Risk Difference (95% CI)	NE	
p-value		
p-value of CMH-Test	NE	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.19.1
Proportion of Participants With Serious Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.19.1
Proportion of Participants With Serious Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.20
Proportion of Participants With Severe Adjudicated Thrombotic Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	19/239 (7.9)	8/232 (3.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	2.31 (1.03, 5.16)	
p-value	0.0423	
Odds Ratio (95% CI)	2.42 (1.04, 5.64)	
p-value	0.0410	
Risk Difference (95% CI)	4.50 (0.35, 8.66)	
p-value	0.0338	
p-value of CMH-Test	0.0358	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.20.1
Proportion of Participants With Severe Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.4344
<65 years	0/ 11 (0.0)	1/ 17 (5.9)	0.50 (0.02, 11.28)	0.6629	
65 - 74 years	2/ 43 (4.7)	2/ 51 (3.9)	1.19 (0.17, 8.07)	0.8615	
>=75 years	17/ 185 (9.2)	5/ 164 (3.0)	3.01 (1.14, 7.99)	0.0265	
Sex					0.5424
Male	10/ 128 (7.8)	5/ 118 (4.2)	1.84 (0.65, 5.24)	0.2507	
Female	9/ 111 (8.1)	3/ 114 (2.6)	3.08 (0.86, 11.08)	0.0849	
Race					0.4984
White	16/ 216 (7.4)	8/ 212 (3.8)	1.96 (0.86, 4.49)	0.1101	
Other	2/ 14 (14.3)	0/ 16 (0.0)	5.67 (0.29, 108.91)	0.2501	
Geographic Region 1					0.3659
North America	2/ 27 (7.4)	2/ 28 (7.1)	1.04 (0.16, 6.85)	0.9699	
Europe	17/ 212 (8.0)	6/ 204 (2.9)	2.73 (1.10, 6.78)	0.0309	
Prior FXa Inhibitor					0.3602
Apixaban	13/ 162 (8.0)	4/ 157 (2.5)	3.15 (1.05, 9.45)	0.0407	
Rivaroxaban	6/ 77 (7.8)	4/ 75 (5.3)	1.46 (0.43, 4.97)	0.5439	
Indication for prior FXa Inhibitor 1					0.2504
Atrial Fibrillation/Flutter	17/ 205 (8.3)	7/ 194 (3.6)	2.30 (0.97, 5.42)	0.0573	
Venous Thromboembolism	2/ 21 (9.5)	0/ 30 (0.0)	7.05 (0.36, 139.66)	0.2001	
Other	0/ 13 (0.0)	1/ 8 (12.5)	0.21 (0.01, 4.71)	0.3284	
Indication for prior FXa Inhibitor 2					0.9827
Atrial Fibrillation/Flutter	17/ 205 (8.3)	7/ 194 (3.6)	2.30 (0.97, 5.42)	0.0573	
Other	2/ 34 (5.9)	1/ 38 (2.6)	2.24 (0.21, 23.57)	0.5033	
Baseline Anti-FXa Activity 1					NE
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)	NE		
>=30 ng/mL	15/ 211 (7.1)	6/ 201 (3.0)	2.38 (0.94, 6.02)	0.0665	
Baseline Anti-FXa Activity 2					0.7954
<75 ng/mL	5/ 67 (7.5)	2/ 52 (3.8)	1.94 (0.39, 9.60)	0.4166	
>=75 ng/mL	10/ 159 (6.3)	4/ 160 (2.5)	2.52 (0.81, 7.85)	0.1123	
ICH Score at baseline					0.7103
< 3	17/ 201 (8.5)	7/ 203 (3.4)	2.45 (1.04, 5.79)	0.0405	
>= 3	2/ 38 (5.3)	1/ 29 (3.4)	1.53 (0.15, 16.03)	0.7245	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.20.1
Proportion of Participants With Severe Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9749
<30 mL	16/ 189 (8.5)	7/ 191 (3.7)	2.31 (0.97, 5.49)	0.0579	
>=30 mL	3/ 50 (6.0)	1/ 40 (2.5)	2.40 (0.26, 22.20)	0.4405	
Baseline Volume of Hematoma 2					0.3545
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)	0.57 (0.03, 12.21)	0.7202	
>=0.5 mL	19/ 233 (8.2)	7/ 220 (3.2)	2.56 (1.10, 5.98)	0.0294	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	15/ 213 (7.0)	8/ 218 (3.7)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.7065
<8 hours	8/ 102 (7.8)	4/ 102 (3.9)	2.00 (0.62, 6.43)	0.2449	
>=8 hours	11/ 131 (8.4)	4/ 130 (3.1)	2.73 (0.89, 8.35)	0.0785	
Intended Usual Care Agent					0.5256
PCC	11/ 158 (7.0)	5/ 156 (3.2)	2.17 (0.77, 6.11)	0.1413	
Other	1/ 18 (5.6)	1/ 11 (9.1)	0.61 (0.04, 8.81)	0.7176	
Unknown	7/ 63 (11.1)	2/ 65 (3.1)	3.61 (0.78, 16.72)	0.1006	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.21
Proportion of Participants With Severe Adjudicated Arterial Systemic Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	2.91 (0.12, 71.13)	
p-value	0.5120	
Odds Ratio (95% CI)	2.92 (0.12, 72.16)	
p-value	0.5118	
Risk Difference (95% CI)	0.42 (-0.40, 1.24)	
p-value	0.3163	
p-value of CMH-Test	0.3245	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.21.1
Proportion of Participants With Severe Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	1/ 185 (0.5)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	1/ 111 (0.9)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	1/ 14 (7.1)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	1/ 212 (0.5)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	1/ 205 (0.5)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	1/ 205 (0.5)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.21.1
Proportion of Participants With Severe Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	1/ 233 (0.4)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	1/ 213 (0.5)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.22
Proportion of Participants With Severe Adjudicated Deep Vein Thrombosis
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.32 (0.01, 7.90)	
p-value	0.4889	
Odds Ratio (95% CI)	0.32 (0.01, 7.95)	
p-value	0.4886	
Risk Difference (95% CI)	-0.43 (-1.27, 0.41)	
p-value	0.3163	
p-value of CMH-Test	0.3101	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.22.1
Proportion of Participants With Severe Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	1/ 51 (2.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	1/ 118 (0.8)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	1/ 212 (0.5)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	1/ 28 (3.6)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	1/ 203 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.22.1
Proportion of Participants With Severe Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	 p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	1/ 220 (0.5)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	1/ 102 (1.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.23
Proportion of Participants With Severe Adjudicated Ischemic Stroke
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	12/239 (5.0)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	3.88 (1.11, 13.58)	
p-value	0.0337	
Odds Ratio (95% CI)	4.04 (1.12, 14.49)	
p-value	0.0324	
Risk Difference (95% CI)	3.73 (0.60, 6.85)	
p-value	0.0195	
p-value of CMH-Test	0.0214	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.23.1
Proportion of Participants With Severe Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.9602
<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
65 - 74 years	1/ 43 (2.3)	0/ 51 (0.0)	3.55 (0.15, 84.86)	0.4347	
>=75 years	11/ 185 (5.9)	3/ 164 (1.8)	3.25 (0.92, 11.45)	0.0665	
Sex					
Male	6/ 128 (4.7)	1/ 118 (0.8)			
Female	6/ 111 (5.4)	2/ 114 (1.8)			
Race					0.9736
White	11/ 216 (5.1)	3/ 212 (1.4)	3.60 (1.02, 12.72)	0.0468	
Other	1/ 14 (7.1)	0/ 16 (0.0)	3.40 (0.15, 77.34)	0.4427	
Geographic Region 1					0.9416
North America	1/ 27 (3.7)	0/ 28 (0.0)	3.11 (0.13, 73.11)	0.4817	
Europe	11/ 212 (5.2)	3/ 204 (1.5)	3.53 (1.00, 12.46)	0.0502	
Prior FXa Inhibitor					0.7718
Apixaban	9/ 162 (5.6)	2/ 157 (1.3)	4.36 (0.96, 19.87)	0.0570	
Rivaroxaban	3/ 77 (3.9)	1/ 75 (1.3)	2.92 (0.31, 27.47)	0.3483	
Indication for prior FXa Inhibitor 1					0.9093
Atrial Fibrillation/Flutter	11/ 205 (5.4)	3/ 194 (1.5)	3.47 (0.98, 12.25)	0.0532	
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
Other	0/ 13 (0.0)	0/ 8 (0.0)	NE		
Indication for prior FXa Inhibitor 2					0.9829
Atrial Fibrillation/Flutter	11/ 205 (5.4)	3/ 194 (1.5)	3.47 (0.98, 12.25)	0.0532	
Other	1/ 34 (2.9)	0/ 38 (0.0)	3.34 (0.14, 79.42)	0.4553	
Baseline Anti-FXa Activity 1					NE
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)	NE		
>=30 ng/mL	9/ 211 (4.3)	3/ 201 (1.5)	2.86 (0.78, 10.41)	0.1113	
Baseline Anti-FXa Activity 2					
<75 ng/mL	2/ 67 (3.0)	2/ 52 (3.8)			
>=75 ng/mL	7/ 159 (4.4)	1/ 160 (0.6)			
ICH Score at baseline					0.2112
< 3	11/ 201 (5.5)	2/ 203 (1.0)	5.55 (1.25, 24.74)	0.0245	
>= 3	1/ 38 (2.6)	1/ 29 (3.4)	0.76 (0.05, 11.69)	0.8461	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.23.1
Proportion of Participants With Severe Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.9156
<30 mL	10/ 189 (5.3)	3/ 191 (1.6)	3.37 (0.94, 12.05)	0.0618	
>=30 mL	2/ 50 (4.0)	0/ 40 (0.0)	4.02 (0.20, 81.42)	0.3647	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	12/ 233 (5.2)	3/ 220 (1.4)	3.78 (1.08, 13.20)	0.0374	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	8/ 213 (3.8)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
Intracranial - subarachnoid	2/ 10 (20.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.4517
<8 hours	4/ 102 (3.9)	0/ 102 (0.0)	9.00 (0.49, 165.04)	0.1388	
>=8 hours	8/ 131 (6.1)	3/ 130 (2.3)	2.65 (0.72, 9.75)	0.1437	
Intended Usual Care Agent					
PCC	5/ 158 (3.2)	2/ 156 (1.3)			
Other	1/ 18 (5.6)	1/ 11 (9.1)			
Unknown	6/ 63 (9.5)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.24
Proportion of Participants With Severe Adjudicated Myocardial Infarction
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	8/239 (3.3)	2/232 (0.9)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	3.88 (0.83, 18.09)	
p-value	0.0840	
Odds Ratio (95% CI)	3.98 (0.84, 18.96)	
p-value	0.0826	
Risk Difference (95% CI)	2.49 (-0.09, 5.06)	
p-value	0.0582	
p-value of CMH-Test	0.0617	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.24.1
Proportion of Participants With Severe Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	1/ 17 (5.9)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	8/ 185 (4.3)	1/ 164 (0.6)			
Sex					
Male	3/ 128 (2.3)	2/ 118 (1.7)			
Female	5/ 111 (4.5)	0/ 114 (0.0)			
Race					
White	7/ 216 (3.2)	2/ 212 (0.9)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	1/ 27 (3.7)	1/ 28 (3.6)			
Europe	7/ 212 (3.3)	1/ 204 (0.5)			
Prior FXa Inhibitor					
Apixaban	6/ 162 (3.7)	1/ 157 (0.6)			
Rivaroxaban	2/ 77 (2.6)	1/ 75 (1.3)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	8/ 205 (3.9)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	1/ 8 (12.5)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	8/ 205 (3.9)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	1/ 38 (2.6)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	7/ 211 (3.3)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	4/ 67 (6.0)	0/ 52 (0.0)			
>=75 ng/mL	3/ 159 (1.9)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	6/ 201 (3.0)	2/ 203 (1.0)			
>= 3	2/ 38 (5.3)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.24.1
Proportion of Participants With Severe Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	7/ 189 (3.7)	1/ 191 (0.5)			
>=30 mL	1/ 50 (2.0)	1/ 40 (2.5)			
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	8/ 233 (3.4)	2/ 220 (0.9)	3.78 (0.81, 17.59)	0.0905	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	7/ 213 (3.3)	2/ 218 (0.9)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 14 (7.1)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	3/ 102 (2.9)	2/ 102 (2.0)			
>=8 hours	5/ 131 (3.8)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	5/ 158 (3.2)	2/ 156 (1.3)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	3/ 63 (4.8)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.25
Proportion of Participants With Severe Adjudicated Pulmonary Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.32 (0.03, 3.09)	
p-value	0.3269	
Odds Ratio (95% CI)	0.32 (0.03, 3.11)	
p-value	0.3263	
Risk Difference (95% CI)	-0.87 (-2.54, 0.79)	
p-value	0.3041	
p-value of CMH-Test	0.3015	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.25.1
Proportion of Participants With Severe Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	1/ 43 (2.3)	2/ 51 (3.9)			
>=75 years	0/ 185 (0.0)	1/ 164 (0.6)			
Sex					
Male	1/ 128 (0.8)	2/ 118 (1.7)			
Female	0/ 111 (0.0)	1/ 114 (0.9)			
Race					
White	1/ 216 (0.5)	3/ 212 (1.4)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	1/ 28 (3.6)			
Europe	1/ 212 (0.5)	2/ 204 (1.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	1/ 157 (0.6)			
Rivaroxaban	1/ 77 (1.3)	2/ 75 (2.7)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	3/ 194 (1.5)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	3/ 194 (1.5)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	1/ 211 (0.5)	2/ 201 (1.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	1/ 159 (0.6)	2/ 160 (1.3)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	3/ 203 (1.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.25.1
Proportion of Participants With Severe Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	3/ 191 (1.6)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	1/ 233 (0.4)	2/ 220 (0.9)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	1/ 213 (0.5)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	2/ 102 (2.0)			
>=8 hours	0/ 131 (0.0)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	1/ 158 (0.6)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	2/ 65 (3.1)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.26
Proportion of Participants With Severe Adjudicated Transient Ischemic Attack
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	NE	
p-value		
Odds Ratio (95% CI)	NE	
p-value		
Risk Difference (95% CI)	NE	
p-value		
p-value of CMH-Test	NE	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.26.1
Proportion of Participants With Severe Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.26.1
Proportion of Participants With Severe Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.27
Proportion of Participants With Non-Severe Adjudicated Thrombotic Events
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	10/239 (4.2)	5/232 (2.2)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.94 (0.67, 5.59)	
p-value	0.2192	
Odds Ratio (95% CI)	1.98 (0.67, 5.89)	
p-value	0.2181	
Risk Difference (95% CI)	2.03 (-1.12, 5.18)	
p-value	0.2071	
p-value of CMH-Test	0.2104	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.27.1
Proportion of Participants With Non-Severe Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	1/ 17 (5.9)			
65 - 74 years	3/ 43 (7.0)	2/ 51 (3.9)			
>=75 years	7/ 185 (3.8)	2/ 164 (1.2)			
Sex					
Male	4/ 128 (3.1)	4/ 118 (3.4)			
Female	6/ 111 (5.4)	1/ 114 (0.9)			
Race					0.7411
White	6/ 216 (2.8)	4/ 212 (1.9)	1.47 (0.42, 5.14)	0.5445	
Other	2/ 14 (14.3)	1/ 16 (6.3)	2.29 (0.23, 22.59)	0.4794	
Geographic Region 1					0.0640
North America	1/ 27 (3.7)	3/ 28 (10.7)	0.35 (0.04, 3.12)	0.3441	
Europe	9/ 212 (4.2)	2/ 204 (1.0)	4.33 (0.95, 19.80)	0.0588	
Prior FXa Inhibitor					0.6984
Apixaban	7/ 162 (4.3)	3/ 157 (1.9)	2.26 (0.60, 8.59)	0.2308	
Rivaroxaban	3/ 77 (3.9)	2/ 75 (2.7)	1.46 (0.25, 8.50)	0.6730	
Indication for prior FXa Inhibitor 1					0.8315
Atrial Fibrillation/Flutter	8/ 205 (3.9)	5/ 194 (2.6)	1.51 (0.50, 4.55)	0.4598	
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
Indication for prior FXa Inhibitor 2					0.4245
Atrial Fibrillation/Flutter	8/ 205 (3.9)	5/ 194 (2.6)	1.51 (0.50, 4.55)	0.4598	
Other	2/ 34 (5.9)	0/ 38 (0.0)	5.57 (0.28, 112.12)	0.2621	
Baseline Anti-FXa Activity 1					0.1803
<30 ng/mL	1/ 15 (6.7)	2/ 11 (18.2)	0.37 (0.04, 3.55)	0.3865	
>=30 ng/mL	7/ 211 (3.3)	3/ 201 (1.5)	2.22 (0.58, 8.48)	0.2422	
Baseline Anti-FXa Activity 2					
<75 ng/mL	5/ 67 (7.5)	3/ 52 (5.8)			
>=75 ng/mL	3/ 159 (1.9)	2/ 160 (1.3)			
ICH Score at baseline					0.1828
< 3	10/ 201 (5.0)	4/ 203 (2.0)	2.52 (0.81, 7.92)	0.1122	
>= 3	0/ 38 (0.0)	1/ 29 (3.4)	0.26 (0.01, 6.07)	0.3993	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.27.1
Proportion of Participants With Non-Severe Adjudicated Thrombotic Events - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.8690
<30 mL	9/ 189 (4.8)	5/ 191 (2.6)	1.82 (0.62, 5.33)	0.2751	
>=30 mL	1/ 50 (2.0)	0/ 40 (0.0)	2.41 (0.10, 57.65)	0.5867	
Baseline Volume of Hematoma 2					0.3950
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)	0.57 (0.03, 12.21)	0.7202	
>=0.5 mL	10/ 233 (4.3)	4/ 220 (1.8)	2.36 (0.75, 7.42)	0.1414	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	9/ 213 (4.2)	5/ 218 (2.3)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	4/ 102 (3.9)	2/ 102 (2.0)			
>=8 hours	5/ 131 (3.8)	3/ 130 (2.3)			
Intended Usual Care Agent					
PCC	5/ 158 (3.2)	4/ 156 (2.6)			
Other	1/ 18 (5.6)	0/ 11 (0.0)			
Unknown	4/ 63 (6.3)	1/ 65 (1.5)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.28
Proportion of Participants With Non-Severe Adjudicated Arterial Systemic Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	2/239 (0.8)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	1.94 (0.18, 21.27)	
p-value	0.5870	
Odds Ratio (95% CI)	1.95 (0.18, 21.65)	
p-value	0.5868	
Risk Difference (95% CI)	0.41 (-1.02, 1.84)	
p-value	0.5780	
p-value of CMH-Test	0.5804	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.28.1
Proportion of Participants With Non-Severe Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	1/ 43 (2.3)	1/ 51 (2.0)			
>=75 years	1/ 185 (0.5)	0/ 164 (0.0)			
Sex					
Male	1/ 128 (0.8)	0/ 118 (0.0)			
Female	1/ 111 (0.9)	1/ 114 (0.9)			
Race					
White	2/ 216 (0.9)	1/ 212 (0.5)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	2/ 212 (0.9)	1/ 204 (0.5)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	1/ 157 (0.6)			
Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	2/ 205 (1.0)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	2/ 205 (1.0)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)			
>=30 ng/mL	1/ 211 (0.5)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	2/ 67 (3.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	2/ 201 (1.0)	1/ 203 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.28.1
Proportion of Participants With Non-Severe Adjudicated Arterial Systemic Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	2/ 189 (1.1)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)			
>=0.5 mL	2/ 233 (0.9)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	2/ 213 (0.9)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	1/ 102 (1.0)			
>=8 hours	1/ 131 (0.8)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	2/ 158 (1.3)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.29
Proportion of Participants With Non-Severe Adjudicated Deep Vein Thrombosis
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	1/239 (0.4)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.97 (0.06, 15.43)	
p-value	0.9832	
Odds Ratio (95% CI)	0.97 (0.06, 15.61)	
p-value	0.9832	
Risk Difference (95% CI)	-0.01 (-1.19, 1.16)	
p-value	0.9832	
p-value of CMH-Test	0.9832	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.29.1
Proportion of Participants With Non-Severe Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	 p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	1/ 185 (0.5)	1/ 164 (0.6)			
Sex					
Male	1/ 128 (0.8)	1/ 118 (0.8)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	1/ 216 (0.5)	1/ 212 (0.5)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	1/ 28 (3.6)			
Europe	1/ 212 (0.5)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	1/ 162 (0.6)	1/ 157 (0.6)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	1/ 194 (0.5)			
Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	1/ 194 (0.5)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	1/ 11 (9.1)			
>=30 ng/mL	1/ 211 (0.5)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	1/ 52 (1.9)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	1/ 201 (0.5)	1/ 203 (0.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.29.1
Proportion of Participants With Non-Severe Adjudicated Deep Vein Thrombosis - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	1/ 189 (0.5)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	1/ 233 (0.4)	1/ 220 (0.5)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	1/ 63 (1.6)	1/ 65 (1.5)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.30
Proportion of Participants With Non-Severe Adjudicated Ischemic Stroke
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	4/239 (1.7)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	8.74 (0.47, 161.39)	
p-value	0.1452	
Odds Ratio (95% CI)	8.89 (0.48, 165.96)	
p-value	0.1436	
Risk Difference (95% CI)	1.67 (0.05, 3.30)	
p-value	0.0437	
p-value of CMH-Test	0.0481	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.30.1
Proportion of Participants With Non-Severe Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	3/ 43 (7.0)	0/ 51 (0.0)			
>=75 years	1/ 185 (0.5)	0/ 164 (0.0)			
Sex					
Male	3/ 128 (2.3)	0/ 118 (0.0)			
Female	1/ 111 (0.9)	0/ 114 (0.0)			
Race					
White	1/ 216 (0.5)	0/ 212 (0.0)			
Other	1/ 14 (7.1)	0/ 16 (0.0)			
Geographic Region 1					
North America	1/ 27 (3.7)	0/ 28 (0.0)			
Europe	3/ 212 (1.4)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	4/ 162 (2.5)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	3/ 205 (1.5)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	1/ 13 (7.7)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	3/ 205 (1.5)	0/ 194 (0.0)			
Other	1/ 34 (2.9)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)			
>=30 ng/mL	3/ 211 (1.4)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	2/ 67 (3.0)	0/ 52 (0.0)			
>=75 ng/mL	2/ 159 (1.3)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	4/ 201 (2.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.30.1
Proportion of Participants With Non-Severe Adjudicated Ischemic Stroke - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	 p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	3/ 189 (1.6)	0/ 191 (0.0)			
>=30 mL	1/ 50 (2.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	4/ 233 (1.7)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	4/ 213 (1.9)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	2/ 102 (2.0)	0/ 102 (0.0)			
>=8 hours	1/ 131 (0.8)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	3/ 158 (1.9)	0/ 156 (0.0)			
Other	1/ 18 (5.6)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.31
Proportion of Participants With Non-Severe Adjudicated Myocardial Infarction
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	4/239 (1.7)	1/232 (0.4)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	3.88 (0.44, 34.48)	
p-value	0.2234	
Odds Ratio (95% CI)	3.93 (0.44, 35.44)	
p-value	0.2223	
Risk Difference (95% CI)	1.24 (-0.59, 3.07)	
p-value	0.1837	
p-value of CMH-Test	0.1888	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.31.1
Proportion of Participants With Non-Severe Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	4/ 185 (2.2)	1/ 164 (0.6)			
Sex					
Male	0/ 128 (0.0)	1/ 118 (0.8)			
Female	4/ 111 (3.6)	0/ 114 (0.0)			
Race					
White	3/ 216 (1.4)	1/ 212 (0.5)			
Other	1/ 14 (7.1)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	1/ 28 (3.6)			
Europe	4/ 212 (1.9)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	2/ 162 (1.2)	1/ 157 (0.6)			
Rivaroxaban	2/ 77 (2.6)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	4/ 205 (2.0)	1/ 194 (0.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	4/ 205 (2.0)	1/ 194 (0.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	2/ 211 (0.9)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	1/ 67 (1.5)	1/ 52 (1.9)			
>=75 ng/mL	1/ 159 (0.6)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	4/ 201 (2.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	1/ 29 (3.4)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.1.31.1
Proportion of Participants With Non-Severe Adjudicated Myocardial Infarction - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	4/ 189 (2.1)	1/ 191 (0.5)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	4/ 233 (1.7)	1/ 220 (0.5)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	4/ 213 (1.9)	1/ 218 (0.5)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	1/ 102 (1.0)	0/ 102 (0.0)			
>=8 hours	3/ 131 (2.3)	1/ 130 (0.8)			
Intended Usual Care Agent					
PCC	1/ 158 (0.6)	1/ 156 (0.6)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	3/ 63 (4.8)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.32
Proportion of Participants With Non-Severe Adjudicated Pulmonary Embolism
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	3/232 (1.3)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.14 (0.01, 2.67)	
p-value	0.1905	
Odds Ratio (95% CI)	0.14 (0.01, 2.66)	
p-value	0.1892	
Risk Difference (95% CI)	-1.29 (-2.75, 0.16)	
p-value	0.0813	
p-value of CMH-Test	0.0781	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.32.1
Proportion of Participants With Non-Severe Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	1/ 17 (5.9)			
65 - 74 years	0/ 43 (0.0)	1/ 51 (2.0)			
>=75 years	0/ 185 (0.0)	1/ 164 (0.6)			
Sex					
Male	0/ 128 (0.0)	3/ 118 (2.5)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	2/ 212 (0.9)			
Other	0/ 14 (0.0)	1/ 16 (6.3)			
Geographic Region 1					
North America	0/ 27 (0.0)	2/ 28 (7.1)			
Europe	0/ 212 (0.0)	1/ 204 (0.5)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	1/ 157 (0.6)			
Rivaroxaban	0/ 77 (0.0)	2/ 75 (2.7)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	3/ 194 (1.5)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	3/ 194 (1.5)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	2/ 11 (18.2)			
>=30 ng/mL	0/ 211 (0.0)	1/ 201 (0.5)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	2/ 52 (3.8)			
>=75 ng/mL	0/ 159 (0.0)	1/ 160 (0.6)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	3/ 203 (1.5)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.32.1
Proportion of Participants With Non-Severe Adjudicated Pulmonary Embolism - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	3/ 191 (1.6)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	3/ 220 (1.4)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	3/ 218 (1.4)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	1/ 102 (1.0)			
>=8 hours	0/ 131 (0.0)	2/ 130 (1.5)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	2/ 156 (1.3)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	1/ 65 (1.5)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.33
Proportion of Participants With Non-Severe Adjudicated Transient Ischemic Attack
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	0/239 (0.0)	0/232 (0.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	NE	
p-value		
Odds Ratio (95% CI)	NE	
p-value		
Risk Difference (95% CI)	NE	
p-value		
p-value of CMH-Test	NE	

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.33.1
Proportion of Participants With Non-Severe Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					
<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
65 - 74 years	0/ 43 (0.0)	0/ 51 (0.0)			
>=75 years	0/ 185 (0.0)	0/ 164 (0.0)			
Sex					
Male	0/ 128 (0.0)	0/ 118 (0.0)			
Female	0/ 111 (0.0)	0/ 114 (0.0)			
Race					
White	0/ 216 (0.0)	0/ 212 (0.0)			
Other	0/ 14 (0.0)	0/ 16 (0.0)			
Geographic Region 1					
North America	0/ 27 (0.0)	0/ 28 (0.0)			
Europe	0/ 212 (0.0)	0/ 204 (0.0)			
Prior FXa Inhibitor					
Apixaban	0/ 162 (0.0)	0/ 157 (0.0)			
Rivaroxaban	0/ 77 (0.0)	0/ 75 (0.0)			
Indication for prior FXa Inhibitor 1					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)			
Other	0/ 13 (0.0)	0/ 8 (0.0)			
Indication for prior FXa Inhibitor 2					
Atrial Fibrillation/Flutter	0/ 205 (0.0)	0/ 194 (0.0)			
Other	0/ 34 (0.0)	0/ 38 (0.0)			
Baseline Anti-FXa Activity 1					
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
>=30 ng/mL	0/ 211 (0.0)	0/ 201 (0.0)			
Baseline Anti-FXa Activity 2					
<75 ng/mL	0/ 67 (0.0)	0/ 52 (0.0)			
>=75 ng/mL	0/ 159 (0.0)	0/ 160 (0.0)			
ICH Score at baseline					
< 3	0/ 201 (0.0)	0/ 203 (0.0)			
>= 3	0/ 38 (0.0)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.1.33.1
Proportion of Participants With Non-Severe Adjudicated Transient Ischemic Attack - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					
<30 mL	0/ 189 (0.0)	0/ 191 (0.0)			
>=30 mL	0/ 50 (0.0)	0/ 40 (0.0)			
Baseline Volume of Hematoma 2					
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)			
>=0.5 mL	0/ 233 (0.0)	0/ 220 (0.0)			
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	0/ 213 (0.0)	0/ 218 (0.0)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	0/ 14 (0.0)	0/ 4 (0.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					
<8 hours	0/ 102 (0.0)	0/ 102 (0.0)			
>=8 hours	0/ 131 (0.0)	0/ 130 (0.0)			
Intended Usual Care Agent					
PCC	0/ 158 (0.0)	0/ 156 (0.0)			
Other	0/ 18 (0.0)	0/ 11 (0.0)			
Unknown	0/ 63 (0.0)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

		Andexanet (N=239)	Usual Care (N=232)
SOC: Blood and lymphatic system disorders	Number of subjects with reponse, n/N (%)	11/239 (4.6)	10/232 (4.3)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.07 (0.46, 2.47)	
	p-value	0.8780	
	Odds Ratio (95% CI)	1.07 (0.45, 2.57)	
	p-value	0.8780	
	Risk Difference (95% CI)	0.29 (-3.43, 4.02)	
	p-value	0.8779	
	p-value of CMH-Test	0.8781	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Cardiac disorders	Number of subjects with reponse, n/N (%)	45/239 (18.8)	28/232 (12.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.56 (1.01, 2.41)	
	p-value	0.0455	
	Odds Ratio (95% CI)	1.69 (1.01, 2.82)	
	p-value	0.0442	
	Risk Difference (95% CI)	6.76 (0.27, 13.25)	
	p-value	0.0413	
	p-value of CMH-Test	0.0429	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Cardiac disorders, PT: Atrial fibrillation	Number of subjects with reponse, n/N (%)	10/239 (4.2)	5/232 (2.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.94 (0.67, 5.59)	
	p-value	0.2192	
	Odds Ratio (95% CI)	1.98 (0.67, 5.89)	
	p-value	0.2181	
	Risk Difference (95% CI)	2.03 (-1.12, 5.18)	
	p-value	0.2071	
	p-value of CMH-Test	0.2104	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Gastrointestinal disorders	Number of subjects with reponse, n/N (%)	68/239 (28.5)	57/232 (24.6)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.16 (0.86, 1.57)	
	p-value	0.3411	
	Odds Ratio (95% CI)	1.22 (0.81, 1.84)	
	p-value	0.3403	
	Risk Difference (95% CI)	3.88 (-4.08, 11.85)	
	p-value	0.3392	
	p-value of CMH-Test	0.3405	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Gastrointestinal disorders, PT: Constipation	Number of subjects with reponse, n/N (%)	37/239 (15.5)	23/232 (9.9)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.56 (0.96, 2.54)	
	p-value	0.0735	
	Odds Ratio (95% CI)	1.66 (0.96, 2.90)	
	p-value	0.0721	
	Risk Difference (95% CI)	5.57 (-0.42, 11.55)	
	p-value	0.0683	
	p-value of CMH-Test	0.0703	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Gastrointestinal disorders, PT: Nausea	Number of subjects with reponse, n/N (%)	22/239 (9.2)	16/232 (6.9)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.33 (0.72, 2.48)	
	p-value	0.3599	
	Odds Ratio (95% CI)	1.37 (0.70, 2.68)	
	p-value	0.3593	
	Risk Difference (95% CI)	2.31 (-2.60, 7.21)	
	p-value	0.3564	
	p-value of CMH-Test	0.3582	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Gastrointestinal disorders, PT: Vomiting	Number of subjects with reponse, n/N (%)	9/239 (3.8)	14/232 (6.0)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.62 (0.28, 1.41)	
	p-value	0.2583	
	Odds Ratio (95% CI)	0.61 (0.26, 1.44)	
	p-value	0.2576	
	Risk Difference (95% CI)	-2.27 (-6.17, 1.63)	
	p-value	0.2543	
	p-value of CMH-Test	0.2539	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: General disorders and administration site conditions	Number of subjects with reponse, n/N (%)	41/239 (17.2)	33/232 (14.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.21 (0.79, 1.84)	
	p-value	0.3834	
	Odds Ratio (95% CI)	1.25 (0.76, 2.06)	
	p-value	0.3828	
	Risk Difference (95% CI)	2.93 (-3.63, 9.49)	
	p-value	0.3813	
	p-value of CMH-Test	0.3827	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: General disorders and administration site conditions, PT: Pyrexia	Number of subjects with reponse, n/N (%)	21/239 (8.8)	19/232 (8.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.07 (0.59, 1.94)	
	p-value	0.8163	
	Odds Ratio (95% CI)	1.08 (0.56, 2.07)	
	p-value	0.8163	
	Risk Difference (95% CI)	0.60 (-4.44, 5.63)	
	p-value	0.8162	
	p-value of CMH-Test	0.8165	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations	Number of subjects with reponse, n/N (%)	126/239 (52.7)	111/232 (47.8)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.10 (0.92, 1.32)	
	p-value	0.2912	
	Odds Ratio (95% CI)	1.22 (0.85, 1.75)	
	p-value	0.2903	
	Risk Difference (95% CI)	4.87 (-4.15, 13.90)	
	p-value	0.2895	
	p-value of CMH-Test	0.2906	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia	Number of subjects with reponse, n/N (%)	37/239 (15.5)	32/232 (13.8)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.12 (0.72, 1.74)	
	p-value	0.6048	
	Odds Ratio (95% CI)	1.14 (0.69, 1.91)	
	p-value	0.6047	
	Risk Difference (95% CI)	1.69 (-4.69, 8.07)	
	p-value	0.6041	
	p-value of CMH-Test	0.6049	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia aspiration	Number of subjects with reponse, n/N (%)	29/239 (12.1)	21/232 (9.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.34 (0.79, 2.28)	
	p-value	0.2801	
	Odds Ratio (95% CI)	1.39 (0.77, 2.51)	
	p-value	0.2792	
	Risk Difference (95% CI)	3.08 (-2.46, 8.63)	
	p-value	0.2761	
	p-value of CMH-Test	0.2782	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Urinary tract infection	Number of subjects with reponse, n/N (%)	48/239 (20.1)	40/232 (17.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.16 (0.80, 1.70)	
	p-value	0.4297	
	Odds Ratio (95% CI)	1.21 (0.76, 1.92)	
	p-value	0.4292	
	Risk Difference (95% CI)	2.84 (-4.19, 9.87)	
	p-value	0.4281	
	p-value of CMH-Test	0.4293	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Injury, poisoning and procedural complications	Number of subjects with reponse, n/N (%)	13/239 (5.4)	12/232 (5.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.05 (0.49, 2.26)	
	p-value	0.8972	
	Odds Ratio (95% CI)	1.05 (0.47, 2.36)	
	p-value	0.8972	
	Risk Difference (95% CI)	0.27 (-3.78, 4.32)	
	p-value	0.8972	
	p-value of CMH-Test	0.8973	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Investigations	Number of subjects with reponse, n/N (%)	19/239 (7.9)	21/232 (9.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.88 (0.49, 1.59)	
	p-value	0.6683	
	Odds Ratio (95% CI)	0.87 (0.45, 1.66)	
	p-value	0.6682	
	Risk Difference (95% CI)	-1.10 (-6.14, 3.94)	
	p-value	0.6682	
	p-value of CMH-Test	0.6683	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Metabolism and nutrition disorders	Number of subjects with reponse, n/N (%)	67/239 (28.0)	45/232 (19.4)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.45 (1.04, 2.01)	
	p-value	0.0296	
	Odds Ratio (95% CI)	1.62 (1.05, 2.49)	
	p-value	0.0284	
	Risk Difference (95% CI)	8.64 (1.00, 16.27)	
	p-value	0.0266	
	p-value of CMH-Test	0.0279	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Metabolism and nutrition disorders, PT: Hypokalaemia	Number of subjects with reponse, n/N (%)	38/239 (15.9)	23/232 (9.9)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.60 (0.99, 2.61)	
	p-value	0.0564	
	Odds Ratio (95% CI)	1.72 (0.99, 2.99)	
	p-value	0.0550	
	Risk Difference (95% CI)	5.99 (-0.04, 12.01)	
	p-value	0.0514	
	p-value of CMH-Test	0.0533	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Musculoskeletal and connective tissue disorders	Number of subjects with reponse, n/N (%)	19/239 (7.9)	10/232 (4.3)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.84 (0.88, 3.88)	
	p-value	0.1069	
	Odds Ratio (95% CI)	1.92 (0.87, 4.22)	
	p-value	0.1055	
	Risk Difference (95% CI)	3.64 (-0.67, 7.95)	
	p-value	0.0981	
	p-value of CMH-Test	0.1008	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders	Number of subjects with reponse, n/N (%)	88/239 (36.8)	80/232 (34.5)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.07 (0.84, 1.36)	
	p-value	0.5968	
	Odds Ratio (95% CI)	1.11 (0.76, 1.61)	
	p-value	0.5966	
	Risk Difference (95% CI)	2.34 (-6.31, 10.99)	
	p-value	0.5963	
	p-value of CMH-Test	0.5969	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Cerebral haemorrhage	Number of subjects with reponse, n/N (%)	8/239 (3.3)	11/232 (4.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.71 (0.29, 1.72)	
	p-value	0.4446	
	Odds Ratio (95% CI)	0.70 (0.27, 1.76)	
	p-value	0.4442	
	Risk Difference (95% CI)	-1.39 (-4.95, 2.17)	
	p-value	0.4429	
	p-value of CMH-Test	0.4425	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Epilepsy	Number of subjects with reponse, n/N (%)	11/239 (4.6)	4/232 (1.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	2.67 (0.86, 8.26)	
	p-value	0.0886	
	Odds Ratio (95% CI)	2.75 (0.86, 8.76)	
	p-value	0.0871	
	Risk Difference (95% CI)	2.88 (-0.26, 6.02)	
	p-value	0.0724	
	p-value of CMH-Test	0.0756	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Haemorrhage intracranial	Number of subjects with reponse, n/N (%)	7/239 (2.9)	10/232 (4.3)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.68 (0.26, 1.75)	
	p-value	0.4248	
	Odds Ratio (95% CI)	0.67 (0.25, 1.79)	
	p-value	0.4244	
	Risk Difference (95% CI)	-1.38 (-4.76, 1.99)	
	p-value	0.4226	
	p-value of CMH-Test	0.4221	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Headache	Number of subjects with reponse, n/N (%)	22/239 (9.2)	18/232 (7.8)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.19 (0.65, 2.15)	
	p-value	0.5741	
	Odds Ratio (95% CI)	1.21 (0.63, 2.31)	
	p-value	0.5739	
	Risk Difference (95% CI)	1.45 (-3.58, 6.47)	
	p-value	0.5729	
	p-value of CMH-Test	0.5739	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Hydrocephalus	Number of subjects with reponse, n/N (%)	10/239 (4.2)	5/232 (2.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.94 (0.67, 5.59)	
	p-value	0.2192	
	Odds Ratio (95% CI)	1.98 (0.67, 5.89)	
	p-value	0.2181	
	Risk Difference (95% CI)	2.03 (-1.12, 5.18)	
	p-value	0.2071	
	p-value of CMH-Test	0.2104	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Ischaemic stroke	Number of subjects with reponse, n/N (%)	14/239 (5.9)	1/232 (0.4)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	13.59 (1.80, 102.52)	
	p-value	0.0114	
	Odds Ratio (95% CI)	14.37 (1.87, 110.21)	
	p-value	0.0103	
	Risk Difference (95% CI)	5.43 (2.33, 8.52)	
	p-value	0.0006	
	p-value of CMH-Test	0.0008	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Psychiatric disorders	Number of subjects with reponse, n/N (%)	55/239 (23.0)	56/232 (24.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.95 (0.69, 1.32)	
	p-value	0.7736	
	Odds Ratio (95% CI)	0.94 (0.61, 1.44)	
	p-value	0.7736	
	Risk Difference (95% CI)	-1.13 (-8.79, 6.54)	
	p-value	0.7736	
	p-value of CMH-Test	0.7738	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Psychiatric disorders, PT: Delirium	Number of subjects with reponse, n/N (%)	20/239 (8.4)	27/232 (11.6)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.72 (0.42, 1.25)	
	p-value	0.2392	
	Odds Ratio (95% CI)	0.69 (0.38, 1.27)	
	p-value	0.2385	
	Risk Difference (95% CI)	-3.27 (-8.69, 2.15)	
	p-value	0.2369	
	p-value of CMH-Test	0.2370	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Psychiatric disorders, PT: Insomnia	Number of subjects with reponse, n/N (%)	14/239 (5.9)	7/232 (3.0)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.94 (0.80, 4.72)	
	p-value	0.1436	
	Odds Ratio (95% CI)	2.00 (0.79, 5.05)	
	p-value	0.1423	
	Risk Difference (95% CI)	2.84 (-0.86, 6.54)	
	p-value	0.1327	
	p-value of CMH-Test	0.1358	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Renal and urinary disorders	Number of subjects with reponse, n/N (%)	30/239 (12.6)	17/232 (7.3)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.71 (0.97, 3.02)	
	p-value	0.0628	
	Odds Ratio (95% CI)	1.82 (0.97, 3.39)	
	p-value	0.0614	
	Risk Difference (95% CI)	5.22 (-0.15, 10.60)	
	p-value	0.0567	
	p-value of CMH-Test	0.0588	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Renal and urinary disorders, PT: Urinary retention	Number of subjects with reponse, n/N (%)	10/239 (4.2)	2/232 (0.9)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	4.85 (1.07, 21.91)	
	p-value	0.0400	
	Odds Ratio (95% CI)	5.02 (1.09, 23.17)	
	p-value	0.0386	
	Risk Difference (95% CI)	3.32 (0.52, 6.13)	
	p-value	0.0202	
	p-value of CMH-Test	0.0223	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with reponse, n/N (%)	43/239 (18.0)	35/232 (15.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.19 (0.79, 1.79)	
	p-value	0.3975	
	Odds Ratio (95% CI)	1.23 (0.76, 2.01)	
	p-value	0.3969	
	Risk Difference (95% CI)	2.91 (-3.80, 9.61)	
	p-value	0.3956	
	p-value of CMH-Test	0.3969	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Skin and subcutaneous tissue disorders	Number of subjects with reponse, n/N (%)	12/239 (5.0)	11/232 (4.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.06 (0.48, 2.35)	
	p-value	0.8881	
	Odds Ratio (95% CI)	1.06 (0.46, 2.46)	
	p-value	0.8881	
	Risk Difference (95% CI)	0.28 (-3.61, 4.17)	
	p-value	0.8880	
	p-value of CMH-Test	0.8882	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Vascular disorders	Number of subjects with reponse, n/N (%)	35/239 (14.6)	25/232 (10.8)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.36 (0.84, 2.20)	
	p-value	0.2108	
	Odds Ratio (95% CI)	1.42 (0.82, 2.46)	
	p-value	0.2096	
	Risk Difference (95% CI)	3.87 (-2.13, 9.87)	
	p-value	0.2064	
	p-value of CMH-Test	0.2085	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Vascular disorders, PT: Hypertension	Number of subjects with reponse, n/N (%)	18/239 (7.5)	12/232 (5.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.46 (0.72, 2.95)	
	p-value	0.2981	
	Odds Ratio (95% CI)	1.49 (0.70, 3.17)	
	p-value	0.2973	
	Risk Difference (95% CI)	2.36 (-2.04, 6.75)	
	p-value	0.2928	
	p-value of CMH-Test	0.2951	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Age					0.0401
	<65 years	1/ 11 (9.1)	2/ 17 (11.8)	0.77 (0.08, 7.54)	0.8244	
	65 - 74 years	3/ 43 (7.0)	9/ 51 (17.6)	0.40 (0.11, 1.37)	0.1431	
	>=75 years	41/ 185 (22.2)	17/ 164 (10.4)	2.14 (1.26, 3.61)	0.0045	
	Sex					0.8583
	Male	23/ 128 (18.0)	13/ 118 (11.0)	1.63 (0.87, 3.07)	0.1295	
	Female	22/ 111 (19.8)	15/ 114 (13.2)	1.51 (0.83, 2.75)	0.1823	
	Race					0.0417
	White	41/ 216 (19.0)	22/ 212 (10.4)	1.83 (1.13, 2.96)	0.0141	
	Other	2/ 14 (14.3)	6/ 16 (37.5)	0.38 (0.09, 1.59)	0.1861	
	Geographic Region 1					0.2363
	North America	5/ 27 (18.5)	6/ 28 (21.4)	0.86 (0.30, 2.50)	0.7878	
	Europe	40/ 212 (18.9)	22/ 204 (10.8)	1.75 (1.08, 2.84)	0.0233	
	Prior FXa Inhibitor					0.4440
	Apixaban	31/ 162 (19.1)	17/ 157 (10.8)	1.77 (1.02, 3.06)	0.0422	
	Rivaroxaban	14/ 77 (18.2)	11/ 75 (14.7)	1.24 (0.60, 2.55)	0.5602	
	Indication for prior FXa Inhibitor 1					0.2106
	Atrial Fibrillation/Flutter	40/ 205 (19.5)	20/ 194 (10.3)	1.89 (1.15, 3.12)	0.0123	
	Venous Thromboembolism	3/ 21 (14.3)	6/ 30 (20.0)	0.71 (0.20, 2.54)	0.6032	
	Other	2/ 13 (15.4)	2/ 8 (25.0)	0.62 (0.11, 3.54)	0.5868	
	Indication for prior FXa Inhibitor 2					0.0847
	Atrial Fibrillation/Flutter	40/ 205 (19.5)	20/ 194 (10.3)	1.89 (1.15, 3.12)	0.0123	
	Other	5/ 34 (14.7)	8/ 38 (21.1)	0.70 (0.25, 1.93)	0.4893	
	Baseline Anti-FXa Activity 1					0.3918
	<30 ng/mL	5/ 15 (33.3)	1/ 11 (9.1)	3.67 (0.50, 27.12)	0.2032	
	>=30 ng/mL	36/ 211 (17.1)	23/ 201 (11.4)	1.49 (0.92, 2.42)	0.1073	
	Baseline Anti-FXa Activity 2					0.0606
	<75 ng/mL	16/ 67 (23.9)	3/ 52 (5.8)	4.14 (1.27, 13.45)	0.0182	
	>=75 ng/mL	25/ 159 (15.7)	21/ 160 (13.1)	1.20 (0.70, 2.05)	0.5098	
	ICH Score at baseline					0.9740
	< 3	37/ 201 (18.4)	24/ 203 (11.8)	1.56 (0.97, 2.50)	0.0678	
	>= 3	8/ 38 (21.1)	4/ 29 (13.8)	1.53 (0.51, 4.58)	0.4506	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Baseline Volume of Hematoma 1					0.3191
	<30 mL	36/ 189 (19.0)	21/ 191 (11.0)	1.73 (1.05, 2.85)	0.0310	
	>=30 mL	9/ 50 (18.0)	7/ 40 (17.5)	1.03 (0.42, 2.52)	0.9509	
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	45/ 233 (19.3)	28/ 220 (12.7)	1.52 (0.98, 2.34)	0.0598	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	42/ 213 (19.7)	28/ 218 (12.8)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					0.0263
	<8 hours	16/ 102 (15.7)	17/ 102 (16.7)	0.94 (0.50, 1.76)	0.8492	
	>=8 hours	29/ 131 (22.1)	11/ 130 (8.5)	2.62 (1.37, 5.01)	0.0037	
	Intended Usual Care Agent					0.8900
	PCC	29/ 158 (18.4)	18/ 156 (11.5)	1.59 (0.92, 2.74)	0.0950	
	Other	6/ 18 (33.3)	2/ 11 (18.2)	1.83 (0.45, 7.54)	0.4007	
	Unknown	10/ 63 (15.9)	8/ 65 (12.3)	1.29 (0.54, 3.06)	0.5633	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Metabolism and nutrition disorders	Age					0.3777
	<65 years	2/ 11 (18.2)	3/ 17 (17.6)	1.03 (0.20, 5.21)	0.9712	
	65 - 74 years	6/ 43 (14.0)	9/ 51 (17.6)	0.79 (0.31, 2.04)	0.6280	
	>=75 years	59/ 185 (31.9)	33/ 164 (20.1)	1.58 (1.09, 2.30)	0.0149	
	Sex					0.6061
	Male	36/ 128 (28.1)	21/ 118 (17.8)	1.58 (0.98, 2.55)	0.0598	
	Female	31/ 111 (27.9)	24/ 114 (21.1)	1.33 (0.83, 2.11)	0.2330	
	Race					0.0896
	White	63/ 216 (29.2)	37/ 212 (17.5)	1.67 (1.17, 2.39)	0.0051	
	Other	3/ 14 (21.4)	6/ 16 (37.5)	0.57 (0.17, 1.87)	0.3550	
	Geographic Region 1					0.5637
	North America	9/ 27 (33.3)	8/ 28 (28.6)	1.17 (0.53, 2.58)	0.7029	
	Europe	58/ 212 (27.4)	37/ 204 (18.1)	1.51 (1.05, 2.17)	0.0272	
	Prior FXa Inhibitor					0.4331
	Apixaban	42/ 162 (25.9)	31/ 157 (19.7)	1.31 (0.87, 1.98)	0.1918	
	Rivaroxaban	25/ 77 (32.5)	14/ 75 (18.7)	1.74 (0.98, 3.08)	0.0578	
	Indication for prior FXa Inhibitor 1					0.2128
	Atrial Fibrillation/Flutter	65/ 205 (31.7)	39/ 194 (20.1)	1.58 (1.12, 2.23)	0.0096	
	Venous Thromboembolism	2/ 21 (9.5)	5/ 30 (16.7)	0.57 (0.12, 2.67)	0.4769	
	Other	0/ 13 (0.0)	1/ 8 (12.5)	0.21 (0.01, 4.71)	0.3284	
	Indication for prior FXa Inhibitor 2					0.0717
	Atrial Fibrillation/Flutter	65/ 205 (31.7)	39/ 194 (20.1)	1.58 (1.12, 2.23)	0.0096	
	Other	2/ 34 (5.9)	6/ 38 (15.8)	0.37 (0.08, 1.72)	0.2065	
	Baseline Anti-FXa Activity 1					0.5337
	<30 ng/mL	4/ 15 (26.7)	3/ 11 (27.3)	0.98 (0.27, 3.51)	0.9725	
	>=30 ng/mL	61/ 211 (28.9)	39/ 201 (19.4)	1.49 (1.05, 2.12)	0.0266	
	Baseline Anti-FXa Activity 2					0.3241
	<75 ng/mL	17/ 67 (25.4)	12/ 52 (23.1)	1.10 (0.58, 2.09)	0.7729	
	>=75 ng/mL	48/ 159 (30.2)	30/ 160 (18.8)	1.61 (1.08, 2.40)	0.0196	
	ICH Score at baseline					0.5870
	< 3	58/ 201 (28.9)	39/ 203 (19.2)	1.50 (1.05, 2.14)	0.0251	
	>= 3	9/ 38 (23.7)	6/ 29 (20.7)	1.14 (0.46, 2.85)	0.7717	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Metabolism and nutrition disorders	Baseline Volume of Hematoma 1					0.8249
	<30 mL	53/ 189 (28.0)	37/ 191 (19.4)	1.45 (1.00, 2.09)	0.0492	
	>=30 mL	14/ 50 (28.0)	7/ 40 (17.5)	1.60 (0.71, 3.58)	0.2533	
	Baseline Volume of Hematoma 2					0.4119
	<0.5 mL	1/ 6 (16.7)	0/ 11 (0.0)	5.14 (0.24, 109.89)	0.2945	
	>=0.5 mL	66/ 233 (28.3)	44/ 220 (20.0)	1.42 (1.01, 1.98)	0.0411	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	61/ 213 (28.6)	44/ 218 (20.2)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	3/ 14 (21.4)	0/ 4 (0.0)			
	Intracranial - subarachnoid	3/ 10 (30.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					0.1630
	<8 hours	24/ 102 (23.5)	22/ 102 (21.6)	1.09 (0.66, 1.82)	0.7377	
	>=8 hours	41/ 131 (31.3)	23/ 130 (17.7)	1.77 (1.13, 2.77)	0.0128	
	Intended Usual Care Agent					0.4819
	PCC	43/ 158 (27.2)	28/ 156 (17.9)	1.52 (0.99, 2.31)	0.0529	
	Other	10/ 18 (55.6)	3/ 11 (27.3)	2.04 (0.71, 5.82)	0.1840	
	Unknown	14/ 63 (22.2)	14/ 65 (21.5)	1.03 (0.54, 1.99)	0.9255	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Age					0.9281
	<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
	65 - 74 years	3/ 43 (7.0)	0/ 51 (0.0)	8.27 (0.44, 155.84)	0.1584	
	>=75 years	11/ 185 (5.9)	1/ 164 (0.6)	9.75 (1.27, 74.72)	0.0284	
	Sex					
	Male	6/ 128 (4.7)	0/ 118 (0.0)			
	Female	8/ 111 (7.2)	1/ 114 (0.9)			
	Race					NE
	White	12/ 216 (5.6)	1/ 212 (0.5)	11.78 (1.55, 89.78)	0.0173	
	Other	0/ 14 (0.0)	0/ 16 (0.0)	NE		
	Geographic Region 1					NE
	North America	0/ 27 (0.0)	0/ 28 (0.0)	NE		
	Europe	14/ 212 (6.6)	1/ 204 (0.5)	13.47 (1.79, 101.52)	0.0116	
	Prior FXa Inhibitor					0.4479
	Apixaban	13/ 162 (8.0)	1/ 157 (0.6)	12.60 (1.67, 95.17)	0.0141	
	Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)	2.92 (0.12, 70.64)	0.5092	
	Indication for prior FXa Inhibitor 1					0.3254
	Atrial Fibrillation/Flutter	13/ 205 (6.3)	1/ 194 (0.5)	12.30 (1.62, 93.15)	0.0151	
	Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
	Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
	Indication for prior FXa Inhibitor 2					0.4970
	Atrial Fibrillation/Flutter	13/ 205 (6.3)	1/ 194 (0.5)	12.30 (1.62, 93.15)	0.0151	
	Other	1/ 34 (2.9)	0/ 38 (0.0)	3.34 (0.14, 79.42)	0.4553	
	Baseline Anti-FXa Activity 1					0.4176
	<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
	>=30 ng/mL	11/ 211 (5.2)	1/ 201 (0.5)	10.48 (1.37, 80.42)	0.0239	
	Baseline Anti-FXa Activity 2					0.7819
	<75 ng/mL	3/ 67 (4.5)	0/ 52 (0.0)	5.46 (0.29, 103.34)	0.2582	
	>=75 ng/mL	9/ 159 (5.7)	1/ 160 (0.6)	9.06 (1.16, 70.65)	0.0355	
	ICH Score at baseline					0.5345
	< 3	12/ 201 (6.0)	1/ 203 (0.5)	12.12 (1.59, 92.34)	0.0160	
	>= 3	2/ 38 (5.3)	0/ 29 (0.0)	3.85 (0.19, 77.16)	0.3786	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Baseline Volume of Hematoma 1					0.7088
	<30 mL	11/ 189 (5.8)	1/ 191 (0.5)	11.12 (1.45, 85.25)	0.0205	
	>=30 mL	3/ 50 (6.0)	0/ 40 (0.0)	5.63 (0.30, 105.87)	0.2485	
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	14/ 233 (6.0)	1/ 220 (0.5)	13.22 (1.75, 99.69)	0.0123	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	12/ 213 (5.6)	1/ 218 (0.5)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					
	<8 hours	5/ 102 (4.9)	0/ 102 (0.0)			
	>=8 hours	8/ 131 (6.1)	1/ 130 (0.8)			
	Intended Usual Care Agent					
	PCC	8/ 158 (5.1)	1/ 156 (0.6)			
	Other	2/ 18 (11.1)	0/ 11 (0.0)			
	Unknown	4/ 63 (6.3)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.1.1
Proportion of Participants with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
SOC: Renal and urinary disorders, PT: Urinary retention	Age					
	<65 years	0/ 11 (0.0)	0/ 17 (0.0)			
	65 - 74 years	2/ 43 (4.7)	1/ 51 (2.0)			
	>=75 years	8/ 185 (4.3)	1/ 164 (0.6)			
	Sex					
	Male	7/ 128 (5.5)	2/ 118 (1.7)			
	Female	3/ 111 (2.7)	0/ 114 (0.0)			
	Race					0.9355
	White	8/ 216 (3.7)	2/ 212 (0.9)	3.93 (0.84, 18.27)	0.0813	
	Other	1/ 14 (7.1)	0/ 16 (0.0)	3.40 (0.15, 77.34)	0.4427	
	Geographic Region 1					0.2226
	North America	1/ 27 (3.7)	1/ 28 (3.6)	1.04 (0.07, 15.76)	0.9791	
	Europe	9/ 212 (4.2)	1/ 204 (0.5)	8.66 (1.11, 67.75)	0.0397	
	Prior FXa Inhibitor					
	Apixaban	7/ 162 (4.3)	1/ 157 (0.6)			
	Rivaroxaban	3/ 77 (3.9)	1/ 75 (1.3)			
	Indication for prior FXa Inhibitor 1					NE
	Atrial Fibrillation/Flutter	10/ 205 (4.9)	2/ 194 (1.0)	4.73 (1.05, 21.32)	0.0430	
	Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
	Other	0/ 13 (0.0)	0/ 8 (0.0)	NE		
	Indication for prior FXa Inhibitor 2					NE
	Atrial Fibrillation/Flutter	10/ 205 (4.9)	2/ 194 (1.0)	4.73 (1.05, 21.32)	0.0430	
	Other	0/ 34 (0.0)	0/ 38 (0.0)	NE		
	Baseline Anti-FXa Activity 1					0.7661
	<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
	>=30 ng/mL	8/ 211 (3.8)	2/ 201 (1.0)	3.81 (0.82, 17.73)	0.0881	
	Baseline Anti-FXa Activity 2					
	<75 ng/mL	3/ 67 (4.5)	0/ 52 (0.0)			
	>=75 ng/mL	6/ 159 (3.8)	2/ 160 (1.3)			
	ICH Score at baseline					0.0561
	< 3	10/ 201 (5.0)	1/ 203 (0.5)	10.10 (1.30, 78.17)	0.0268	
	>= 3	0/ 38 (0.0)	1/ 29 (3.4)	0.26 (0.01, 6.07)	0.3993	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
SOC: Renal and urinary disorders, PT: Urinary retention	Baseline Volume of Hematoma 1					
	<30 mL	9/ 189 (4.8)	0/ 191 (0.0)			
	>=30 mL	1/ 50 (2.0)	2/ 40 (5.0)			
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	10/ 233 (4.3)	2/ 220 (0.9)	4.72 (1.05, 21.31)	0.0435	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	8/ 213 (3.8)	2/ 218 (0.9)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					
	<8 hours	3/ 102 (2.9)	2/ 102 (2.0)			
	>=8 hours	6/ 131 (4.6)	0/ 130 (0.0)			
	Intended Usual Care Agent					
	PCC	6/ 158 (3.8)	2/ 156 (1.3)			
	Other	1/ 18 (5.6)	0/ 11 (0.0)			
	Unknown	3/ 63 (4.8)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Cardiac disorders	Number of subjects with reponse, n/N (%)	21/239 (8.8)	4/232 (1.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	5.10 (1.78, 14.62)	
	p-value	0.0025	
	Odds Ratio (95% CI)	5.49 (1.85, 16.25)	
	p-value	0.0021	
	Risk Difference (95% CI)	7.06 (3.10, 11.02)	
	p-value	0.0005	
	p-value of CMH-Test	0.0006	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations	Number of subjects with reponse, n/N (%)	37/239 (15.5)	27/232 (11.6)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.33 (0.84, 2.11)	
	p-value	0.2261	
	Odds Ratio (95% CI)	1.39 (0.82, 2.37)	
	p-value	0.2250	
	Risk Difference (95% CI)	3.84 (-2.33, 10.01)	
	p-value	0.2221	
	p-value of CMH-Test	0.2241	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia	Number of subjects with reponse, n/N (%)	11/239 (4.6)	15/232 (6.5)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.71 (0.33, 1.52)	
	p-value	0.3787	
	Odds Ratio (95% CI)	0.70 (0.31, 1.55)	
	p-value	0.3783	
	Risk Difference (95% CI)	-1.86 (-5.99, 2.27)	
	p-value	0.3768	
	p-value of CMH-Test	0.3766	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia aspiration	Number of subjects with reponse, n/N (%)	11/239 (4.6)	7/232 (3.0)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.53 (0.60, 3.87)	
	p-value	0.3736	
	Odds Ratio (95% CI)	1.55 (0.59, 4.07)	
	p-value	0.3731	
	Risk Difference (95% CI)	1.59 (-1.86, 5.04)	
	p-value	0.3678	
	p-value of CMH-Test	0.3701	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders	Number of subjects with reponse, n/N (%)	45/239 (18.8)	44/232 (19.0)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.99 (0.68, 1.44)	
	p-value	0.9697	
	Odds Ratio (95% CI)	0.99 (0.62, 1.57)	
	p-value	0.9697	
	Risk Difference (95% CI)	-0.14 (-7.21, 6.93)	
	p-value	0.9697	
	p-value of CMH-Test	0.9697	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Cerebral haemorrhage	Number of subjects with reponse, n/N (%)	7/239 (2.9)	11/232 (4.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.62 (0.24, 1.57)	
	p-value	0.3101	
	Odds Ratio (95% CI)	0.61 (0.23, 1.59)	
	p-value	0.3095	
	Risk Difference (95% CI)	-1.81 (-5.28, 1.66)	
	p-value	0.3061	
	p-value of CMH-Test	0.3055	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Ischaemic stroke	Number of subjects with reponse, n/N (%)	12/239 (5.0)	1/232 (0.4)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	11.65 (1.53, 88.87)	
	p-value	0.0179	
	Odds Ratio (95% CI)	12.21 (1.57, 94.69)	
	p-value	0.0166	
	Risk Difference (95% CI)	4.59 (1.70, 7.48)	
	p-value	0.0019	
	p-value of CMH-Test	0.0024	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with reponse, n/N (%)	16/239 (6.7)	12/232 (5.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.29 (0.63, 2.68)	
	p-value	0.4864	
	Odds Ratio (95% CI)	1.32 (0.61, 2.84)	
	p-value	0.4860	
	Risk Difference (95% CI)	1.52 (-2.74, 5.78)	
	p-value	0.4839	
	p-value of CMH-Test	0.4854	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.2.1
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Age					0.3249
	<65 years	1/ 11 (9.1)	1/ 17 (5.9)	1.55 (0.11, 22.23)	0.7489	
	65 - 74 years	1/ 43 (2.3)	1/ 51 (2.0)	1.19 (0.08, 18.40)	0.9029	
	>=75 years	19/ 185 (10.3)	2/ 164 (1.2)	8.42 (1.99, 35.61)	0.0038	
	Sex					0.7134
	Male	9/ 128 (7.0)	2/ 118 (1.7)	4.15 (0.91, 18.81)	0.0651	
	Female	12/ 111 (10.8)	2/ 114 (1.8)	6.16 (1.41, 26.91)	0.0156	
	Race					0.2581
	White	19/ 216 (8.8)	3/ 212 (1.4)	6.22 (1.87, 20.70)	0.0029	
	Other	1/ 14 (7.1)	1/ 16 (6.3)	1.14 (0.08, 16.63)	0.9221	
	Geographic Region 1					0.4222
	North America	2/ 27 (7.4)	1/ 28 (3.6)	2.07 (0.20, 21.56)	0.5414	
	Europe	19/ 212 (9.0)	3/ 204 (1.5)	6.09 (1.83, 20.28)	0.0032	
	Prior FXa Inhibitor					0.6559
	Apixaban	13/ 162 (8.0)	2/ 157 (1.3)	6.30 (1.44, 27.46)	0.0143	
	Rivaroxaban	8/ 77 (10.4)	2/ 75 (2.7)	3.90 (0.86, 17.75)	0.0788	
	Indication for prior FXa Inhibitor 1					0.3036
	Atrial Fibrillation/Flutter	19/ 205 (9.3)	3/ 194 (1.5)	5.99 (1.80, 19.93)	0.0035	
	Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
	Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
	Indication for prior FXa Inhibitor 2					0.4647
	Atrial Fibrillation/Flutter	19/ 205 (9.3)	3/ 194 (1.5)	5.99 (1.80, 19.93)	0.0035	
	Other	2/ 34 (5.9)	1/ 38 (2.6)	2.24 (0.21, 23.57)	0.5033	
	Baseline Anti-FXa Activity 1					0.6075
	<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
	>=30 ng/mL	17/ 211 (8.1)	3/ 201 (1.5)	5.40 (1.61, 18.14)	0.0064	
	Baseline Anti-FXa Activity 2					0.5612
	<75 ng/mL	6/ 67 (9.0)	0/ 52 (0.0)	10.13 (0.58, 175.86)	0.1118	
	>=75 ng/mL	12/ 159 (7.5)	3/ 160 (1.9)	4.03 (1.16, 13.99)	0.0285	
	ICH Score at baseline					0.8917
	< 3	19/ 201 (9.5)	4/ 203 (2.0)	4.80 (1.66, 13.85)	0.0038	
	>= 3	2/ 38 (5.3)	0/ 29 (0.0)	3.85 (0.19, 77.16)	0.3786	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2.1
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Baseline Volume of Hematoma 1					0.8101
	<30 mL	16/ 189 (8.5)	3/ 191 (1.6)	5.39 (1.60, 18.19)	0.0067	
	>=30 mL	5/ 50 (10.0)	1/ 40 (2.5)	4.00 (0.49, 32.87)	0.1971	
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	21/ 233 (9.0)	4/ 220 (1.8)	4.96 (1.73, 14.21)	0.0029	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	18/ 213 (8.5)	4/ 218 (1.8)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					0.1218
	<8 hours	9/ 102 (8.8)	4/ 102 (3.9)	2.25 (0.72, 7.07)	0.1652	
	>=8 hours	12/ 131 (9.2)	0/ 130 (0.0)	24.81 (1.48, 414.73)	0.0254	
	Intended Usual Care Agent					0.9365
	PCC	12/ 158 (7.6)	3/ 156 (1.9)	3.95 (1.14, 13.72)	0.0307	
	Other	3/ 18 (16.7)	0/ 11 (0.0)	4.42 (0.25, 78.26)	0.3107	
	Unknown	6/ 63 (9.5)	1/ 65 (1.5)	6.19 (0.77, 49.97)	0.0871	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.2.1
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Age					0.8271
	<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
	65 - 74 years	2/ 43 (4.7)	0/ 51 (0.0)	5.91 (0.29, 119.84)	0.2473	
	>=75 years	10/ 185 (5.4)	1/ 164 (0.6)	8.86 (1.15, 68.51)	0.0365	
	Sex					
	Male	6/ 128 (4.7)	0/ 118 (0.0)			
	Female	6/ 111 (5.4)	1/ 114 (0.9)			
	Race					NE
	White	11/ 216 (5.1)	1/ 212 (0.5)	10.80 (1.41, 82.89)	0.0222	
	Other	0/ 14 (0.0)	0/ 16 (0.0)	NE		
	Geographic Region 1					NE
	North America	0/ 27 (0.0)	0/ 28 (0.0)	NE		
	Europe	12/ 212 (5.7)	1/ 204 (0.5)	11.55 (1.52, 88.00)	0.0182	
	Prior FXa Inhibitor					0.5023
	Apixaban	11/ 162 (6.8)	1/ 157 (0.6)	10.66 (1.39, 81.60)	0.0227	
	Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)	2.92 (0.12, 70.64)	0.5092	
	Indication for prior FXa Inhibitor 1					0.3719
	Atrial Fibrillation/Flutter	11/ 205 (5.4)	1/ 194 (0.5)	10.41 (1.36, 79.87)	0.0242	
	Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
	Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
	Indication for prior FXa Inhibitor 2					0.5545
	Atrial Fibrillation/Flutter	11/ 205 (5.4)	1/ 194 (0.5)	10.41 (1.36, 79.87)	0.0242	
	Other	1/ 34 (2.9)	0/ 38 (0.0)	3.34 (0.14, 79.42)	0.4553	
	Baseline Anti-FXa Activity 1					0.4821
	<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
	>=30 ng/mL	9/ 211 (4.3)	1/ 201 (0.5)	8.57 (1.10, 67.06)	0.0406	
	Baseline Anti-FXa Activity 2					
	<75 ng/mL	3/ 67 (4.5)	0/ 52 (0.0)			
	>=75 ng/mL	7/ 159 (4.4)	1/ 160 (0.6)			
	ICH Score at baseline					0.6022
	< 3	10/ 201 (5.0)	1/ 203 (0.5)	10.10 (1.30, 78.17)	0.0268	
	>= 3	2/ 38 (5.3)	0/ 29 (0.0)	3.85 (0.19, 77.16)	0.3786	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.2.1
Proportion of Participants with frequent Serious Adverse Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Baseline Volume of Hematoma 1					0.7929
	<30 mL	9/ 189 (4.8)	1/ 191 (0.5)	9.10 (1.16, 71.09)	0.0353	
	>=30 mL	3/ 50 (6.0)	0/ 40 (0.0)	5.63 (0.30, 105.87)	0.2485	
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	12/ 233 (5.2)	1/ 220 (0.5)	11.33 (1.49, 86.41)	0.0192	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	10/ 213 (4.7)	1/ 218 (0.5)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					
	<8 hours	5/ 102 (4.9)	0/ 102 (0.0)			
	>=8 hours	7/ 131 (5.3)	1/ 130 (0.8)			
	Intended Usual Care Agent					
	PCC	6/ 158 (3.8)	1/ 156 (0.6)			
	Other	2/ 18 (11.1)	0/ 11 (0.0)			
	Unknown	4/ 63 (6.3)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Cardiac disorders	Number of subjects with reponse, n/N (%)	18/239 (7.5)	5/232 (2.2)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	3.49 (1.32, 9.26)	
	p-value	0.0118	
	Odds Ratio (95% CI)	3.70 (1.35, 10.13)	
	p-value	0.0110	
	Risk Difference (95% CI)	5.38 (1.54, 9.21)	
	p-value	0.0060	
	p-value of CMH-Test	0.0069	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations	Number of subjects with reponse, n/N (%)	33/239 (13.8)	28/232 (12.1)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.14 (0.71, 1.83)	
	p-value	0.5747	
	Odds Ratio (95% CI)	1.17 (0.68, 2.00)	
	p-value	0.5745	
	Risk Difference (95% CI)	1.74 (-4.32, 7.80)	
	p-value	0.5738	
	p-value of CMH-Test	0.5747	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia	Number of subjects with reponse, n/N (%)	11/239 (4.6)	15/232 (6.5)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.71 (0.33, 1.52)	
	p-value	0.3787	
	Odds Ratio (95% CI)	0.70 (0.31, 1.55)	
	p-value	0.3783	
	Risk Difference (95% CI)	-1.86 (-5.99, 2.27)	
	p-value	0.3768	
	p-value of CMH-Test	0.3766	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Infections and infestations, PT: Pneumonia aspiration	Number of subjects with reponse, n/N (%)	11/239 (4.6)	8/232 (3.4)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.33 (0.55, 3.26)	
	p-value	0.5261	
	Odds Ratio (95% CI)	1.35 (0.53, 3.42)	
	p-value	0.5258	
	Risk Difference (95% CI)	1.15 (-2.39, 4.70)	
	p-value	0.5234	
	p-value of CMH-Test	0.5249	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders	Number of subjects with reponse, n/N (%)	47/239 (19.7)	44/232 (19.0)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.04 (0.72, 1.50)	
	p-value	0.8475	
	Odds Ratio (95% CI)	1.05 (0.66, 1.65)	
	p-value	0.8475	
	Risk Difference (95% CI)	0.70 (-6.43, 7.83)	
	p-value	0.8475	
	p-value of CMH-Test	0.8477	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Cerebral haemorrhage	Number of subjects with reponse, n/N (%)	7/239 (2.9)	11/232 (4.7)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	0.62 (0.24, 1.57)	
	p-value	0.3101	
	Odds Ratio (95% CI)	0.61 (0.23, 1.59)	
	p-value	0.3095	
	Risk Difference (95% CI)	-1.81 (-5.28, 1.66)	
	p-value	0.3061	
	p-value of CMH-Test	0.3055	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Nervous system disorders, PT: Ischaemic stroke	Number of subjects with reponse, n/N (%)	10/239 (4.2)	1/232 (0.4)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	9.71 (1.25, 75.23)	
	p-value	0.0296	
	Odds Ratio (95% CI)	10.09 (1.28, 79.44)	
	p-value	0.0282	
	Risk Difference (95% CI)	3.75 (1.08, 6.43)	
	p-value	0.0060	
	p-value of CMH-Test	0.0071	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.3
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

		Andexanet (N=239)	Usual Care (N=232)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with reponse, n/N (%)	16/239 (6.7)	13/232 (5.6)
	Analysis Andexanet vs. Usual Care		
	Relative Risk (95% CI)	1.19 (0.59, 2.43)	
	p-value	0.6229	
	Odds Ratio (95% CI)	1.21 (0.57, 2.57)	
	p-value	0.6228	
	Risk Difference (95% CI)	1.09 (-3.24, 5.43)	
	p-value	0.6218	
	p-value of CMH-Test	0.6227	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Table 4.2.3.1
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Age					0.3012
	<65 years	0/ 11 (0.0)	1/ 17 (5.9)	0.50 (0.02, 11.28)	0.6629	
	65 - 74 years	1/ 43 (2.3)	1/ 51 (2.0)	1.19 (0.08, 18.40)	0.9029	
	>=75 years	17/ 185 (9.2)	3/ 164 (1.8)	5.02 (1.50, 16.83)	0.0089	
	Sex					0.7685
	Male	9/ 128 (7.0)	2/ 118 (1.7)	4.15 (0.91, 18.81)	0.0651	
	Female	9/ 111 (8.1)	3/ 114 (2.6)	3.08 (0.86, 11.08)	0.0849	
	Race					0.0496
	White	17/ 216 (7.9)	3/ 212 (1.4)	5.56 (1.65, 18.70)	0.0055	
	Other	0/ 14 (0.0)	2/ 16 (12.5)	0.23 (0.01, 4.36)	0.3250	
	Geographic Region 1					0.6383
	North America	2/ 27 (7.4)	1/ 28 (3.6)	2.07 (0.20, 21.56)	0.5414	
	Europe	16/ 212 (7.5)	4/ 204 (2.0)	3.85 (1.31, 11.32)	0.0143	
	Prior FXa Inhibitor					0.2846
	Apixaban	12/ 162 (7.4)	2/ 157 (1.3)	5.81 (1.32, 25.56)	0.0198	
	Rivaroxaban	6/ 77 (7.8)	3/ 75 (4.0)	1.95 (0.51, 7.51)	0.3326	
	Indication for prior FXa Inhibitor 1					0.2085
	Atrial Fibrillation/Flutter	17/ 205 (8.3)	4/ 194 (2.1)	4.02 (1.38, 11.74)	0.0109	
	Venous Thromboembolism	1/ 21 (4.8)	0/ 30 (0.0)	4.23 (0.18, 99.01)	0.3703	
	Other	0/ 13 (0.0)	1/ 8 (12.5)	0.21 (0.01, 4.71)	0.3284	
	Indication for prior FXa Inhibitor 2					0.3925
	Atrial Fibrillation/Flutter	17/ 205 (8.3)	4/ 194 (2.1)	4.02 (1.38, 11.74)	0.0109	
	Other	1/ 34 (2.9)	1/ 38 (2.6)	1.12 (0.07, 17.19)	0.9364	
	Baseline Anti-FXa Activity 1					0.7539
	<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
	>=30 ng/mL	16/ 211 (7.6)	4/ 201 (2.0)	3.81 (1.30, 11.20)	0.0151	
	Baseline Anti-FXa Activity 2					0.5065
	<75 ng/mL	5/ 67 (7.5)	0/ 52 (0.0)	8.57 (0.48, 151.62)	0.1427	
	>=75 ng/mL	12/ 159 (7.5)	4/ 160 (2.5)	3.02 (0.99, 9.16)	0.0511	
	ICH Score at baseline					0.7152
	< 3	15/ 201 (7.5)	5/ 203 (2.5)	3.03 (1.12, 8.18)	0.0287	
	>= 3	3/ 38 (7.9)	0/ 29 (0.0)	5.38 (0.29, 100.31)	0.2592	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.3.1
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Cardiac disorders	Baseline Volume of Hematoma 1					0.8709
	<30 mL	13/ 189 (6.9)	4/ 191 (2.1)	3.28 (1.09, 9.89)	0.0345	
	>=30 mL	5/ 50 (10.0)	1/ 40 (2.5)	4.00 (0.49, 32.87)	0.1971	
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	18/ 233 (7.7)	5/ 220 (2.3)	3.40 (1.28, 9.00)	0.0138	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	16/ 213 (7.5)	5/ 218 (2.3)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					0.2502
	<8 hours	9/ 102 (8.8)	4/ 102 (3.9)	2.25 (0.72, 7.07)	0.1652	
	>=8 hours	9/ 131 (6.9)	1/ 130 (0.8)	8.93 (1.15, 69.49)	0.0365	
	Intended Usual Care Agent					0.9680
	PCC	12/ 158 (7.6)	4/ 156 (2.6)	2.96 (0.98, 8.99)	0.0551	
	Other	3/ 18 (16.7)	0/ 11 (0.0)	4.42 (0.25, 78.26)	0.3107	
	Unknown	3/ 63 (4.8)	1/ 65 (1.5)	3.10 (0.33, 28.97)	0.3221	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.3.1
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Age					0.6743
	<65 years	0/ 11 (0.0)	0/ 17 (0.0)	NE		
	65 - 74 years	1/ 43 (2.3)	0/ 51 (0.0)	3.55 (0.15, 84.86)	0.4347	
	>=75 years	9/ 185 (4.9)	1/ 164 (0.6)	7.98 (1.02, 62.30)	0.0477	
	Sex					
	Male	4/ 128 (3.1)	0/ 118 (0.0)			
	Female	6/ 111 (5.4)	1/ 114 (0.9)			
	Race					NE
	White	10/ 216 (4.6)	1/ 212 (0.5)	9.81 (1.27, 76.00)	0.0287	
	Other	0/ 14 (0.0)	0/ 16 (0.0)	NE		
	Geographic Region 1					NE
	North America	0/ 27 (0.0)	0/ 28 (0.0)	NE		
	Europe	10/ 212 (4.7)	1/ 204 (0.5)	9.62 (1.24, 74.50)	0.0301	
	Prior FXa Inhibitor					0.5718
	Apixaban	9/ 162 (5.6)	1/ 157 (0.6)	8.72 (1.12, 68.04)	0.0388	
	Rivaroxaban	1/ 77 (1.3)	0/ 75 (0.0)	2.92 (0.12, 70.64)	0.5092	
	Indication for prior FXa Inhibitor 1					NE
	Atrial Fibrillation/Flutter	10/ 205 (4.9)	1/ 194 (0.5)	9.46 (1.22, 73.23)	0.0313	
	Venous Thromboembolism	0/ 21 (0.0)	0/ 30 (0.0)	NE		
	Other	0/ 13 (0.0)	0/ 8 (0.0)	NE		
	Indication for prior FXa Inhibitor 2					NE
	Atrial Fibrillation/Flutter	10/ 205 (4.9)	1/ 194 (0.5)	9.46 (1.22, 73.23)	0.0313	
	Other	0/ 34 (0.0)	0/ 38 (0.0)	NE		
	Baseline Anti-FXa Activity 1					
	<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)			
	>=30 ng/mL	8/ 211 (3.8)	1/ 201 (0.5)			
	Baseline Anti-FXa Activity 2					
	<75 ng/mL	2/ 67 (3.0)	0/ 52 (0.0)			
	>=75 ng/mL	6/ 159 (3.8)	1/ 160 (0.6)			
	ICH Score at baseline					
	< 3	8/ 201 (4.0)	1/ 203 (0.5)			
	>= 3	2/ 38 (5.3)	0/ 29 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.2.3.1
Proportion of Participants with frequent Severe Adverse Event (CTCAE Grade >=3) by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

	Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
SOC: Nervous system disorders, PT: Ischaemic stroke	Baseline Volume of Hematoma 1					
	<30 mL	7/ 189 (3.7)	1/ 191 (0.5)			
	>=30 mL	3/ 50 (6.0)	0/ 40 (0.0)			
	Baseline Volume of Hematoma 2					NE
	<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
	>=0.5 mL	10/ 233 (4.3)	1/ 220 (0.5)	9.44 (1.22, 73.15)	0.0316	
	Index Bleeding Location 1					
	Intracranial - intracerebral hemorrhage	8/ 213 (3.8)	1/ 218 (0.5)			
	Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
	Intracranial - subdural	2/ 14 (14.3)	0/ 4 (0.0)			
	Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
	Time to Randomization since the last FXa Inhibitor Dose					
	<8 hours	3/ 102 (2.9)	0/ 102 (0.0)			
	>=8 hours	7/ 131 (5.3)	1/ 130 (0.8)			
	Intended Usual Care Agent					
	PCC	4/ 158 (2.5)	1/ 156 (0.6)			
	Other	2/ 18 (11.1)	0/ 11 (0.0)			
	Unknown	4/ 63 (6.3)	0/ 65 (0.0)			

Analysis based on Treatment-Emergent Adverse Events (TEAEs). SOC, PT coded using MedDRA version 25.1
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.1
Analysis of Time from Initial Hospitalization to Discharge (in days)
Safety Analysis Set

	Andexanet (N=238)	Usual Care (N=233)
N	211	199
Mean (SD)	13.07 (8.917)	12.24 (8.058)
LSMean (SE)	12.88 (0.593)	12.07 (0.608)
Analysis Andexanet vs. Usual Care		
Difference of LSMeans (95% CI)	0.81 (-0.83, 2.46)	
p-value	0.3323	
Hedges'g (95% CI)	0.09 (-0.10, 0.29)	
p-value	0.3390	

Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.1.1
Analysis of Time from Initial Hospitalization to Discharge (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Age								0.5560
<65 years	11	15.43 (3.37)	15	10.07 (3.08)	5.36 (-3.98, 14.69)	0.2474	0.45 (-0.34, 1.24)	
65 - 74 years	37	13.75 (1.31)	47	12.96 (1.22)	0.79 (-2.68, 4.25)	0.6533	0.09 (-0.34, 0.53)	
>=75 years	163	12.48 (0.67)	137	12.10 (0.72)	0.37 (-1.55, 2.29)	0.7026	0.04 (-0.18, 0.27)	
Sex								0.7023
Male	116	12.51 (0.78)	103	11.99 (0.82)	0.52 (-1.66, 2.70)	0.6367	0.06 (-0.20, 0.33)	
Female	95	13.39 (0.92)	96	12.22 (0.91)	1.17 (-1.36, 3.70)	0.3629	0.13 (-0.15, 0.41)	
Race								0.0007
White	195	13.30 (0.62)	184	11.80 (0.64)	1.50 (-0.22, 3.22)	0.0876	0.17 (-0.03, 0.38)	
Other	11	7.41 (2.18)	13	16.42 (2.03)	-9.01 (-15.18, -2.85)	0.0062	-1.19 (-2.08, -0.31)	
Geographic Region 1								0.7993
North America	24	12.79 (2.02)	20	11.20 (2.35)	1.59 (-4.67, 7.85)	0.6102	0.15 (-0.44, 0.75)	
Europe	187	12.91 (0.62)	179	12.14 (0.63)	0.77 (-0.94, 2.49)	0.3764	0.09 (-0.11, 0.30)	
Prior FXa Inhibitor								0.0083
Apixaban	143	13.40 (0.72)	133	11.05 (0.74)	2.34 (0.32, 4.36)	0.0234	0.27 (0.04, 0.51)	
Rivaroxaban	68	11.83 (1.04)	66	14.13 (1.06)	-2.30 (-5.12, 0.53)	0.1100	-0.27 (-0.61, 0.08)	
Indication for prior FXa Inhibitor 1								0.9479
Atrial Fibrillation/Flutter	180	13.06 (0.65)	166	12.41 (0.68)	0.65 (-1.18, 2.49)	0.4853	0.07 (-0.14, 0.29)	
Venous Thromboembolism	20	10.83 (1.72)	25	9.81 (1.37)	1.02 (-3.24, 5.28)	0.6316	0.14 (-0.45, 0.73)	
Other	11	13.68 (2.74)	8	11.73 (3.25)	1.94 (-7.02, 10.91)	0.6521	0.20 (-0.71, 1.12)	
Indication for prior FXa Inhibitor 2								0.7197
Atrial Fibrillation/Flutter	180	13.06 (0.65)	166	12.41 (0.68)	0.65 (-1.18, 2.49)	0.4853	0.07 (-0.14, 0.29)	
Other	31	11.71 (1.42)	33	10.31 (1.32)	1.41 (-2.36, 5.18)	0.4587	0.18 (-0.31, 0.67)	
Baseline Anti-FXa Activity 1								0.7746
<30 ng/mL	14	14.34 (1.85)	7	14.59 (2.45)	-0.25 (-6.60, 6.10)	0.9350	-0.04 (-0.94, 0.87)	
>=30 ng/mL	187	12.78 (0.65)	175	12.13 (0.67)	0.65 (-1.15, 2.46)	0.4758	0.07 (-0.13, 0.28)	
Baseline Anti-FXa Activity 2								0.7873
<75 ng/mL	59	13.29 (1.12)	47	13.03 (1.24)	0.26 (-3.01, 3.53)	0.8753	0.03 (-0.35, 0.41)	
>=75 ng/mL	142	12.72 (0.74)	135	11.94 (0.76)	0.79 (-1.27, 2.85)	0.4523	0.09 (-0.15, 0.32)	
ICH Score at baseline								0.6974
< 3	180	13.00 (0.61)	173	12.02 (0.62)	0.98 (-0.69, 2.66)	0.2490	0.12 (-0.09, 0.33)	
>= 3	31	12.20 (2.05)	26	12.43 (2.23)	-0.22 (-6.22, 5.77)	0.9405	-0.02 (-0.54, 0.50)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.1.1
Analysis of Time from Initial Hospitalization to Discharge (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Baseline Volume of Hematoma 1								0.9598
<30 mL	168	13.18 (0.64)	162	12.25 (0.65)	0.93 (-0.84, 2.69)	0.3021	0.11 (-0.10, 0.33)	
>=30 mL	43	11.78 (1.53)	36	10.98 (1.65)	0.81 (-3.65, 5.26)	0.7196	0.08 (-0.36, 0.52)	
Baseline Volume of Hematoma 2								0.1057
<0.5 mL	6	12.41 (1.67)	10	8.14 (1.44)	4.27 (-0.23, 8.77)	0.0609	0.92 (-0.16, 1.99)	
>=0.5 mL	205	12.89 (0.61)	188	12.27 (0.63)	0.62 (-1.08, 2.33)	0.4726	0.07 (-0.13, 0.27)	
Index Bleeding Location 1								
Intracranial - intracerebral hemorrhage	185		185					
Intracranial - intraventricular hemorrhage	2		1					
Intracranial - subdural	14		4					
Intracranial - subarachnoid	10		8					
Time to Randomization since the last FXa Inhibitor Dose								0.1080
<8 hours	94	14.17 (0.97)	85	11.75 (1.03)	2.42 (-0.28, 5.12)	0.0787	0.26 (-0.04, 0.55)	
>=8 hours	113	12.04 (0.76)	114	12.40 (0.75)	-0.36 (-2.45, 1.73)	0.7332	-0.04 (-0.31, 0.22)	
Intended Usual Care Agent								0.3101
PCC	134	12.73 (0.79)	135	12.09 (0.77)	0.64 (-1.49, 2.76)	0.5555	0.07 (-0.17, 0.31)	
Other	16	17.52 (2.81)	9	10.88 (3.44)	6.64 (-2.43, 15.71)	0.1430	0.59 (-0.25, 1.42)	
Unknown	61	11.96 (0.91)	55	12.25 (0.97)	-0.29 (-2.93, 2.35)	0.8275	-0.04 (-0.40, 0.32)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.2
Analysis of Time Spent in Intensive Care Unit (in days)
Safety Analysis Set

	Andexanet (N=238)	Usual Care (N=233)
N	120	115
Mean (SD)	9.91 (7.062)	8.47 (7.624)
LSMean (SE)	9.72 (0.665)	8.28 (0.679)
Analysis Andexanet vs. Usual Care		
Difference of LSMeans (95% CI)	1.44 (-0.43, 3.30)	
p-value	0.1302	
Hedges'g (95% CI)	0.20 (-0.06, 0.45)	
p-value	0.1332	

Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.2.1
Analysis of Time Spent in Intensive Care Unit (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Age								0.8683
<65 years	6	7.46 (3.21)	11	6.79 (2.70)	0.67 (-7.77, 9.12)	0.8667	0.07 (-0.92, 1.07)	
65 - 74 years	23	9.91 (1.57)	28	9.41 (1.45)	0.50 (-3.77, 4.77)	0.8139	0.06 (-0.49, 0.62)	
>=75 years	91	9.80 (0.76)	76	8.11 (0.83)	1.70 (-0.52, 3.92)	0.1330	0.23 (-0.07, 0.54)	
Sex								0.1228
Male	72	8.83 (0.90)	58	8.70 (0.99)	0.13 (-2.50, 2.75)	0.9231	0.02 (-0.33, 0.36)	
Female	48	10.88 (0.99)	57	7.83 (0.92)	3.05 (0.37, 5.73)	0.0260	0.44 (0.05, 0.83)	
Race								0.0290
White	104	10.29 (0.72)	104	8.19 (0.71)	2.10 (0.12, 4.08)	0.0376	0.29 (0.01, 0.56)	
Other	10	4.80 (2.36)	8	11.12 (2.76)	-6.32 (-14.26, 1.62)	0.1104	-0.79 (-1.77, 0.18)	
Geographic Region 1								0.6512
North America	11	10.51 (2.03)	14	7.96 (1.84)	2.55 (-3.16, 8.26)	0.3649	0.36 (-0.44, 1.16)	
Europe	109	9.58 (0.71)	101	8.36 (0.73)	1.22 (-0.77, 3.22)	0.2286	0.17 (-0.11, 0.44)	
Prior FXa Inhibitor								0.0173
Apixaban	80	10.32 (0.74)	74	7.14 (0.77)	3.18 (1.07, 5.28)	0.0034	0.48 (0.16, 0.80)	
Rivaroxaban	40	8.41 (1.33)	41	10.24 (1.31)	-1.83 (-5.45, 1.78)	0.3154	-0.22 (-0.65, 0.22)	
Indication for prior FXa Inhibitor 1								0.8416
Atrial Fibrillation/Flutter	103	9.70 (0.74)	91	8.47 (0.79)	1.23 (-0.89, 3.36)	0.2538	0.16 (-0.12, 0.45)	
Venous Thromboembolism	10	9.75 (1.91)	19	7.77 (1.36)	1.98 (-2.77, 6.73)	0.3998	0.32 (-0.45, 1.09)	
Other	7	10.46 (2.87)	5	6.75 (3.41)	3.71 (-6.45, 13.86)	0.4304	0.45 (-0.72, 1.62)	
Indication for prior FXa Inhibitor 2								0.6437
Atrial Fibrillation/Flutter	103	9.70 (0.74)	91	8.47 (0.79)	1.23 (-0.89, 3.36)	0.2538	0.16 (-0.12, 0.45)	
Other	17	9.81 (1.51)	24	7.55 (1.27)	2.27 (-1.70, 6.23)	0.2544	0.36 (-0.27, 0.98)	
Baseline Anti-FXa Activity 1								0.8645
<30 ng/mL	9	10.95 (3.01)	4	8.75 (4.34)	2.20 (-9.58, 13.99)	0.6857	0.23 (-0.95, 1.41)	
>=30 ng/mL	103	9.64 (0.74)	101	8.35 (0.74)	1.28 (-0.76, 3.33)	0.2174	0.17 (-0.10, 0.45)	
Baseline Anti-FXa Activity 2								0.1617
<75 ng/mL	35	9.56 (1.38)	29	10.48 (1.50)	-0.92 (-4.98, 3.14)	0.6516	-0.11 (-0.60, 0.38)	
>=75 ng/mL	77	9.85 (0.82)	76	7.50 (0.83)	2.35 (0.06, 4.63)	0.0442	0.32 (0.00, 0.64)	
ICH Score at baseline								0.3370
< 3	103	9.33 (0.71)	99	8.28 (0.72)	1.05 (-0.94, 3.03)	0.2994	0.15 (-0.13, 0.42)	
>= 3	17	12.08 (1.92)	16	8.20 (2.01)	3.88 (-1.78, 9.53)	0.1717	0.47 (-0.22, 1.17)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

AstraZeneca
Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.2.1
Analysis of Time Spent in Intensive Care Unit (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Baseline Volume of Hematoma 1								0.7506
<30 mL	94	9.67 (0.74)	89	8.28 (0.77)	1.38 (-0.71, 3.47)	0.1932	0.19 (-0.10, 0.48)	
>=30 mL	26	9.95 (1.53)	25	7.80 (1.54)	2.15 (-2.21, 6.51)	0.3268	0.27 (-0.28, 0.83)	
Baseline Volume of Hematoma 2								0.1765
<0.5 mL	6	9.25 (1.84)	6	4.25 (1.84)	5.00 (-0.71, 10.71)	0.0789	1.02 (-0.21, 2.26)	
>=0.5 mL	114	9.76 (0.69)	108	8.42 (0.71)	1.34 (-0.59, 3.27)	0.1735	0.18 (-0.08, 0.45)	
Index Bleeding Location 1								
Intracranial - intracerebral hemorrhage	101		106					
Intracranial - intraventricular hemorrhage	1		1					
Intracranial - subdural	9		3					
Intracranial - subarachnoid	9		4					
Time to Randomization since the last FXa Inhibitor Dose								0.0951
<8 hours	54	11.17 (1.01)	54	8.04 (1.02)	3.13 (0.33, 5.92)	0.0285	0.42 (0.03, 0.80)	
>=8 hours	62	8.50 (0.92)	61	8.58 (0.92)	-0.08 (-2.66, 2.51)	0.9522	-0.01 (-0.36, 0.34)	
Intended Usual Care Agent								0.7691
PCC	70	9.38 (0.85)	80	8.07 (0.79)	1.31 (-0.97, 3.60)	0.2584	0.18 (-0.14, 0.50)	
Other	11	14.01 (3.18)	2	9.50 (6.77)	4.51 (-12.15, 21.17)	0.5600	0.40 (-1.12, 1.92)	
Unknown	39	8.97 (1.17)	33	8.81 (1.28)	0.16 (-3.31, 3.63)	0.9264	0.02 (-0.44, 0.49)	

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.3
Proportion of Participants With Re-hospitalization
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	17/239 (7.1)	7/232 (3.0)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	2.36 (1.00, 5.58)	
p-value	0.0510	
Odds Ratio (95% CI)	2.46 (1.00, 6.05)	
p-value	0.0497	
Risk Difference (95% CI)	4.10 (0.16, 8.03)	
p-value	0.0412	
p-value of CMH-Test	0.0435	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.3.1
Proportion of Participants With Re-hospitalization - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.9092
<65 years	2/ 11 (18.2)	1/ 17 (5.9)	3.09 (0.32, 30.14)	0.3315	
65 - 74 years	3/ 43 (7.0)	2/ 51 (3.9)	1.78 (0.31, 10.16)	0.5170	
>=75 years	12/ 185 (6.5)	4/ 164 (2.4)	2.66 (0.87, 8.09)	0.0847	
Sex					0.7371
Male	9/ 128 (7.0)	3/ 118 (2.5)	2.77 (0.77, 9.97)	0.1200	
Female	8/ 111 (7.2)	4/ 114 (3.5)	2.05 (0.64, 6.63)	0.2285	
Race					0.5662
White	16/ 216 (7.4)	6/ 212 (2.8)	2.62 (1.04, 6.56)	0.0402	
Other	1/ 14 (7.1)	1/ 16 (6.3)	1.14 (0.08, 16.63)	0.9221	
Geographic Region 1					0.9081
North America	2/ 27 (7.4)	1/ 28 (3.6)	2.07 (0.20, 21.56)	0.5414	
Europe	15/ 212 (7.1)	6/ 204 (2.9)	2.41 (0.95, 6.08)	0.0635	
Prior FXa Inhibitor					0.6083
Apixaban	13/ 162 (8.0)	6/ 157 (3.8)	2.10 (0.82, 5.39)	0.1228	
Rivaroxaban	4/ 77 (5.2)	1/ 75 (1.3)	3.90 (0.45, 34.06)	0.2189	
Indication for prior FXa Inhibitor 1					0.3824
Atrial Fibrillation/Flutter	13/ 205 (6.3)	6/ 194 (3.1)	2.05 (0.80, 5.29)	0.1373	
Venous Thromboembolism	3/ 21 (14.3)	0/ 30 (0.0)	9.86 (0.54, 181.50)	0.1235	
Other	1/ 13 (7.7)	1/ 8 (12.5)	0.62 (0.04, 8.52)	0.7173	
Indication for prior FXa Inhibitor 2					0.5142
Atrial Fibrillation/Flutter	13/ 205 (6.3)	6/ 194 (3.1)	2.05 (0.80, 5.29)	0.1373	
Other	4/ 34 (11.8)	1/ 38 (2.6)	4.47 (0.52, 38.07)	0.1706	
Baseline Anti-FXa Activity 1					NE
<30 ng/mL	0/ 15 (0.0)	0/ 11 (0.0)	NE		
>=30 ng/mL	15/ 211 (7.1)	6/ 201 (3.0)	2.38 (0.94, 6.02)	0.0665	
Baseline Anti-FXa Activity 2					0.2177
<75 ng/mL	6/ 67 (9.0)	0/ 52 (0.0)	10.13 (0.58, 175.86)	0.1118	
>=75 ng/mL	9/ 159 (5.7)	6/ 160 (3.8)	1.51 (0.55, 4.14)	0.4240	
ICH Score at baseline					0.9998
< 3	16/ 201 (8.0)	7/ 203 (3.4)	2.31 (0.97, 5.49)	0.0585	
>= 3	1/ 38 (2.6)	0/ 29 (0.0)	2.31 (0.10, 54.67)	0.6046	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Table 4.3.3.1
Proportion of Participants With Re-hospitalization - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.2261
<30 mL	15/ 189 (7.9)	5/ 191 (2.6)	3.03 (1.12, 8.18)	0.0284	
>=30 mL	2/ 50 (4.0)	2/ 40 (5.0)	0.80 (0.12, 5.43)	0.8194	
Baseline Volume of Hematoma 2					0.3436
<0.5 mL	0/ 6 (0.0)	1/ 11 (9.1)	0.57 (0.03, 12.21)	0.7202	
>=0.5 mL	17/ 233 (7.3)	6/ 220 (2.7)	2.68 (1.07, 6.66)	0.0345	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	15/ 213 (7.0)	6/ 218 (2.8)			
Intracranial - intraventricular hemorrhage	0/ 2 (0.0)	0/ 1 (0.0)			
Intracranial - subdural	1/ 14 (7.1)	1/ 4 (25.0)			
Intracranial - subarachnoid	1/ 10 (10.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.2022
<8 hours	3/ 102 (2.9)	3/ 102 (2.9)	1.00 (0.21, 4.84)	1.0000	
>=8 hours	14/ 131 (10.7)	4/ 130 (3.1)	3.47 (1.17, 10.27)	0.0244	
Intended Usual Care Agent					0.9303
PCC	12/ 158 (7.6)	5/ 156 (3.2)	2.37 (0.85, 6.57)	0.0972	
Other	0/ 18 (0.0)	0/ 11 (0.0)	NE		
Unknown	5/ 63 (7.9)	2/ 65 (3.1)	2.58 (0.52, 12.81)	0.2466	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.4
Analysis of Total Duration of Re-hospitalization (in days)
Safety Analysis Set

	Andexanet (N=238)	Usual Care (N=233)
N	14	7
Mean (SD)	7.79 (7.547)	3.14 (1.676)
LSMean (SE)	8.03 (1.771)	3.50 (2.513)
Analysis Andexanet vs. Usual Care		
Difference of LSMeans (95% CI)	4.52 (-1.75, 10.79)	
p-value	0.1469	
Hedges'g (95% CI)	0.65 (-0.28, 1.59)	
p-value	0.1693	

Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Andexanet Alfa - Study ANNEXA-I - Clinical Data Lock Date: 18 September 2023
Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.4.1
Analysis of Total Duration of Re-hospitalization (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Age								
<65 years	2		1					
65 - 74 years	2		2					
>=75 years	10		4					
Sex								0.9816
Male	7	9.21 (3.57)	3	5.79 (6.46)	3.42 (-13.44, 20.28)	0.6464	0.31 (-1.05, 1.68)	
Female	7	6.59 (1.34)	4	3.00 (1.66)	3.59 (-1.34, 8.51)	0.1314	0.95 (-0.38, 2.27)	
Race								
White	13		6					
Other	1		1					
Geographic Region 1								
North America	2		1					
Europe	12		6					
Prior FXa Inhibitor								
Apixaban	11		6					
Rivaroxaban	3		1					
Indication for prior FXa Inhibitor 1								
Atrial Fibrillation/Flutter	11		6					
Venous Thromboembolism	2		0					
Other	1		1					
Indication for prior FXa Inhibitor 2								
Atrial Fibrillation/Flutter	11		6					
Other	3		1					
Baseline Anti-FXa Activity 1								
<30 ng/mL	0		0					
>=30 ng/mL	12		6					
Baseline Anti-FXa Activity 2								
<75 ng/mL	5		0					
>=75 ng/mL	7		6					
ICH Score at baseline								
< 3	13		7					
>= 3	1		0					

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.3.4.1
Analysis of Total Duration of Re-hospitalization (in days) - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet (N=238) N	Andexanet (N=238) LSMean (SE)	Usual Care (N=233) N	Usual Care (N=233) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedges'g (95% CI)	Interaction p-Value
Baseline Volume of Hematoma 1								
<30 mL	12		5					
>=30 mL	2		2					
Baseline Volume of Hematoma 2								
<0.5 mL	0		1					
>=0.5 mL	14		6					
Index Bleeding Location 1								
Intracranial - intracerebral hemorrhage	12		6					
Intracranial - intraventricular hemorrhage	0		0					
Intracranial - subdural	1		1					
Intracranial - subarachnoid	1		0					
Time to Randomization since the last FXa Inhibitor Dose								
<8 hours	3		3					
>=8 hours	11		4					
Intended Usual Care Agent								
PCC	9		5					
Other	0		0					
Unknown	5		2					

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Estimates are obtained from GLM with treatment arm, time from symptom onset to baseline imaging scan (<180 minutes vs. >=180 minutes) as the covariates.
N describes number of patients included in the GLM.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
SE: Standard Error; CI=Confidence Interval, LSMean = Least Squares Mean, GLM = Generalized Linear Model.

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Table 4.4.1
Proportion of Participants With Post-Randomization Invasive Intracranial Procedures
Safety Analysis Set

	Andexanet (N=239)	Usual Care (N=232)
Number of subjects with reponse, n/N (%)	16/239 (6.7)	20/232 (8.6)
Analysis Andexanet vs. Usual Care		
Relative Risk (95% CI)	0.78 (0.41, 1.46)	
p-value	0.4330	
Odds Ratio (95% CI)	0.76 (0.38, 1.51)	
p-value	0.4327	
Risk Difference (95% CI)	-1.93 (-6.73, 2.88)	
p-value	0.4320	
p-value of CMH-Test	0.4320	

RR, OR and RD estimated using Mantel-Haenszel method or, in case of zero events (RR and OR only), Logit method including correction of 0.5 in every cell of those tables that contain a zero.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.4.1.1
Proportion of Participants With Post-Randomization Invasive Intracranial Procedures - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Age					0.8687
<65 years	1/ 11 (9.1)	1/ 17 (5.9)	1.55 (0.11, 22.23)	0.7489	
65 - 74 years	5/ 43 (11.6)	7/ 51 (13.7)	0.85 (0.29, 2.48)	0.7620	
>=75 years	10/ 185 (5.4)	12/ 164 (7.3)	0.74 (0.33, 1.66)	0.4651	
Sex					0.4305
Male	8/ 128 (6.3)	12/ 118 (10.2)	0.61 (0.26, 1.45)	0.2666	
Female	8/ 111 (7.2)	8/ 114 (7.0)	1.03 (0.40, 2.64)	0.9559	
Race					0.7681
White	15/ 216 (6.9)	18/ 212 (8.5)	0.82 (0.42, 1.58)	0.5496	
Other	1/ 14 (7.1)	2/ 16 (12.5)	0.57 (0.06, 5.65)	0.6321	
Geographic Region 1					0.7041
North America	3/ 27 (11.1)	5/ 28 (17.9)	0.62 (0.16, 2.35)	0.4845	
Europe	13/ 212 (6.1)	15/ 204 (7.4)	0.83 (0.41, 1.71)	0.6199	
Prior FXa Inhibitor					0.3871
Apixaban	11/ 162 (6.8)	11/ 157 (7.0)	0.97 (0.43, 2.17)	0.9393	
Rivaroxaban	5/ 77 (6.5)	9/ 75 (12.0)	0.54 (0.19, 1.54)	0.2498	
Indication for prior FXa Inhibitor 1					0.6780
Atrial Fibrillation/Flutter	15/ 205 (7.3)	18/ 194 (9.3)	0.79 (0.41, 1.52)	0.4783	
Venous Thromboembolism	0/ 21 (0.0)	2/ 30 (6.7)	0.28 (0.01, 5.59)	0.4059	
Other	1/ 13 (7.7)	0/ 8 (0.0)	1.93 (0.09, 42.35)	0.6769	
Indication for prior FXa Inhibitor 2					0.7825
Atrial Fibrillation/Flutter	15/ 205 (7.3)	18/ 194 (9.3)	0.79 (0.41, 1.52)	0.4783	
Other	1/ 34 (2.9)	2/ 38 (5.3)	0.56 (0.05, 5.89)	0.6282	
Baseline Anti-FXa Activity 1					0.4940
<30 ng/mL	1/ 15 (6.7)	0/ 11 (0.0)	2.25 (0.10, 50.54)	0.6095	
>=30 ng/mL	14/ 211 (6.6)	18/ 201 (9.0)	0.74 (0.38, 1.45)	0.3812	
Baseline Anti-FXa Activity 2					0.5128
<75 ng/mL	6/ 67 (9.0)	8/ 52 (15.4)	0.58 (0.22, 1.57)	0.2863	
>=75 ng/mL	9/ 159 (5.7)	10/ 160 (6.3)	0.91 (0.38, 2.17)	0.8240	
ICH Score at baseline					0.2740
< 3	12/ 201 (6.0)	13/ 203 (6.4)	0.93 (0.44, 1.99)	0.8565	
>= 3	4/ 38 (10.5)	7/ 29 (24.1)	0.44 (0.14, 1.35)	0.1498	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

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Extended Population excluding Participants receiving Edoxaban or Enoxaparin
Table 4.4.1.1
Proportion of Participants With Post-Randomization Invasive Intracranial Procedures - Subgroup analysis
Safety Analysis Set

Subgroup Level	Andexanet n/ N (%)	Usual Care n/ N (%)	Andexanet vs. Usual Care RR (95% CI)	Andexanet vs. Usual Care p-Value	Interaction p-Value
Baseline Volume of Hematoma 1					0.7959
<30 mL	9/ 189 (4.8)	11/ 191 (5.8)	0.83 (0.35, 1.95)	0.6639	
>=30 mL	7/ 50 (14.0)	8/ 40 (20.0)	0.70 (0.28, 1.77)	0.4499	
Baseline Volume of Hematoma 2					NE
<0.5 mL	0/ 6 (0.0)	0/ 11 (0.0)	NE		
>=0.5 mL	16/ 233 (6.9)	19/ 220 (8.6)	0.80 (0.42, 1.51)	0.4819	
Index Bleeding Location 1					
Intracranial - intracerebral hemorrhage	13/ 213 (6.1)	18/ 218 (8.3)			
Intracranial - intraventricular hemorrhage	1/ 2 (50.0)	0/ 1 (0.0)			
Intracranial - subdural	2/ 14 (14.3)	1/ 4 (25.0)			
Intracranial - subarachnoid	0/ 10 (0.0)	0/ 8 (0.0)			
Time to Randomization since the last FXa Inhibitor Dose					0.8810
<8 hours	10/ 102 (9.8)	13/ 102 (12.7)	0.77 (0.35, 1.67)	0.5083	
>=8 hours	6/ 131 (4.6)	7/ 130 (5.4)	0.85 (0.29, 2.46)	0.7655	
Intended Usual Care Agent					0.8384
PCC	11/ 158 (7.0)	14/ 156 (9.0)	0.78 (0.36, 1.66)	0.5115	
Other	1/ 18 (5.6)	0/ 11 (0.0)	1.89 (0.08, 42.82)	0.6879	
Unknown	4/ 63 (6.3)	6/ 65 (9.2)	0.69 (0.20, 2.32)	0.5467	

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or, in case of zero events, Logit method including correction of 0.5 in every cell of those tables that contain a zero.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable