2.7.6 Synopsis of Individual Studies : Appendix

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A.1 Study 2001

Table A.1-1 Study 2001: Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class Preferred Term	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Any Adverse Event	3	(33.3)	4	6	(42.9)	9	5	(55.6)	9	5	(33.3)	7	16	(64.0)	29
Musculoskeletal and connective tissue disorders	0		0	2	(14.3)	3	3	(33.3)	4	1	(6.7)	2	6	(24.0)	9
Arthralgia	0		0	1	(7.1)	1	2	(22.2)	3	1	(6.7)	1	4	(16.0)	5
Back pain	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Joint range of motion decreased	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Myalgia	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Pain in extremity	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Injury, poisoning and procedural complications	2	(22.2)	2	2	(14.3)	2	1	(11.1)	1	1	(6.7)	1	5	(20.0)	6
Joint injury	1	(11.1)	1	0		0	1	(11.1)	1	0		0	2	(8.0)	2
Limb injury	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Muscle rupture	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Muscle strain	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
General disorders and administration site conditions	0		0	2	(14.3)	2	1	(11.1)	2	0		0	3	(12.0)	4
Feeling hot	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Inflammation	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Injection site erythema	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Injection site haematoma	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment.
Source: Listing 16.2.7.2
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System Organ Class Preferred Term	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Nervous system disorders	0		0	1	(7.1)	1	1	(11.1)	1	2	(13.3)	2	3	(12.0)	4
Headache	0		0	1	(7.1)	1	1	(11.1)	1	1	(6.7)	1	2	(8.0)	3
Dizziness	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Infections and infestations	1	(11.1)	1	1	(7.1)	1	0		0	1	(6.7)	1	3	(12.0)	3
Nasopharyngitis	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Influenza	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Gastrointestinal disorders	1	(11.1)	1	0		0	1	(11.1)	1	0		0	2	(8.0)	2
Abdominal pain	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Constipation	1	(11.1)	1	0		0	0		0	0		0	1	(4.0)	1
Vascular disorders	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Peripheral coldness	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment.
Source: Listing 16.2.7.2
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Source: Table 14.3.2.1.

Table A.1-2 Study 2001: Summary of Treatment-Emergent Adverse Events by System Organ Class Preferred Term, and Maximum Relationship to Study Treatment (Safety Population)

System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Any Adverse Event	3	(33.3)	4	6	(42.9)	9	5	(55.6)	9	5	(33.3)	7	16	(64.0)	29
Not related	2	(22.2)	3	5	(35.7)	7	4	(44.4)	8	4	(26.7)	5	12	(48.0)	23
Unlikely related	0		0	0		0	0		0	1	(6.7)	2	1	(4.0)	2
Possibly related	1	(11.1)	1	1	(7.1)	2	1	(11.1)	1	0		0	3	(12.0)	4
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Musculoskeletal and connective tissue disorders	0		0	2	(14.3)	3	3	(33.3)	4	1	(6.7)	2	6	(24.0)	9
Not related	0		0	2	(14.3)	3	3	(33.3)	4	1	(6.7)	2	6	(24.0)	9
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Arthralgia	0		0	1	(7.1)	1	2	(22.2)	3	1	(6.7)	1	4	(16.0)	5
Not related	0		0	1	(7.1)	1	2	(22.2)	3	1	(6.7)	1	4	(16.0)	5
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related
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Source: Listing 16.2.7.2
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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Back pain	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Not related	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Joint range of motion decreased	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Myalgia	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Not related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

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Source: Listing 16.2.7.2

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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Pain in extremity	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Not related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Injury, poisoning and procedural complications	2	(22.2)	2	2	(14.3)	2	1	(11.1)	1	1	(6.7)	1	5	(20.0)	6
Not related	2	(22.2)	2	2	(14.3)	2	1	(11.1)	1	1	(6.7)	1	5	(20.0)	6
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Joint injury	1	(11.1)	1	0		0	1	(11.1)	1	0		0	2	(8.0)	2
Not related	1	(11.1)	1	0		0	1	(11.1)	1	0		0	2	(8.0)	2
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

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Source: Listing 16.2.7.2

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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Limb injury	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Not related	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Muscle rupture	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Not related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Muscle strain	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

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Source: Listing 16.2.7.2

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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
General disorders and administration site conditions	0		0	2	(14.3)	2	1	(11.1)	2	0		0	3	(12.0)	4
Not related	0		0	1	(7.1)	1	0		1	0		0	1	(4.0)	2
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	1	(7.1)	1	1	(11.1)	1	0		0	2	(8.0)	2
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Feeling hot	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Inflammation	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Not related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related
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Source: Listing 16.2.7.2
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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Injection site erythema	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Injection site haematoma	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Not related	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Nervous system disorders	0		0	1	(7.1)	1	1	(11.1)	1	2	(13.3)	2	3	(12.0)	4
Not related	0		0	0		0	1	(11.1)	1	1	(6.7)	1	1	(4.0)	2
Unlikely related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Possibly related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

.
Source: Listing 16.2.7.2
Chiltern • [redacted]20[redacted]:10:04 AM • K:\CSL_Behring\29570\21_Stat\Programs\Tables\t_aebygrp.sas

System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Headache	0		0	1	(7.1)	1	1	(11.1)	1	1	(6.7)	1	2	(8.0)	3
Not related	0		0	0		0	1	(11.1)	1	1	(6.7)	1	1	(4.0)	2
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	1	(7.1)	1	0		0	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Dizziness	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Infections and infestations	1	(11.1)	1	1	(7.1)	1	0		0	1	(6.7)	1	3	(12.0)	3
Not related	1	(11.1)	1	1	(7.1)	1	0		0	1	(6.7)	1	3	(12.0)	3
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

.
Source: Listing 16.2.7.2
Chiltern • [redacted]20[redacted]:10:04 AM • K:\CSL_Behring\29570\21_Stat\Programs\Tables\t_aebygrp.sas

System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Nasopharyngitis	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Not related	1	(11.1)	1	1	(7.1)	1	0		0	0		0	2	(8.0)	2
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Influenza	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Gastrointestinal disorders	1	(11.1)	1	0		0	1	(11.1)	1	0		0	2	(8.0)	2
Not related	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	1	(11.1)	1	0		0	0		0	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

.
Source: Listing 16.2.7.2
Chiltern • [redacted]:10:04 AM • K:\CSL_Behring\29570\21_Stat\Programs\Tables\t_aebygrp.sas

System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Abdominal pain	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Not related	0		0	0		0	1	(11.1)	1	0		0	1	(4.0)	1
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Constipation	1	(11.1)	1	0		0	0		0	0		0	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	0		0	0		0
Possibly related	1	(11.1)	1	0		0	0		0	0		0	1	(4.0)	1
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0
Vascular disorders	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

.

Source: Listing 16.2.7.2

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System Organ Class Preferred Term Relationship	25 IU/kg rIX-FP (N=9)			50 IU/kg rIX-FP (N=14)			75 IU/kg rIX-FP (N=9)			50 IU/kg FIX (N=15)			Total (N=25)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Peripheral coldness	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Not related	0		0	0		0	0		0	0		0	0		0
Unlikely related	0		0	0		0	0		0	1	(6.7)	1	1	(4.0)	1
Possibly related	0		0	0		0	0		0	0		0	0		0
Probably related	0		0	0		0	0		0	0		0	0		0
Related	0		0	0		0	0		0	0		0	0		0

Notes: Adverse events are coded using MedDRA version 13.1. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count at the maximum relationship to treatment. Events are counted each time in the event (E) column. Percentages are based on the number of subjects in the safety population in each dose group. AEs are attributed to the treatment the subject was receiving when the AE began. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related

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Source: Listing 16.2.7.2
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Source: Table 14.3.2.3.

A.2 Study 2004

Table A.2-1 Study 2004: Summary Statistics of Uncorrected FIX Activity in Plasma (IU/dL) (PK Population)

Time Point	Prophylaxis Treatment (N=10)	On-Demand Treatment (N=3)	Overall Treatment (N=13)
Day 1, Prior to dosing			
n	10	3	13
Mean (SD)	2.31 (1.091)	0.23 (0.231)	1.83 (1.316)
Median	2.20	0.10	1.70
25%, 75%	1.40, 3.40	0.10, 0.50	1.00, 2.70
Min, Max	1.0, 4.1	0.1, 0.5	0.1, 4.1
Day 1, 30 min post dose			
n	10	3	13
Mean (SD)	39.16 (3.535)	33.90 (1.836)	37.95 (3.906)
Median	39.25	33.10	37.00
25%, 75%	36.60, 41.60	32.60, 36.00	35.80, 41.00
Min, Max	33.3, 44.7	32.6, 36.0	32.6, 44.7
Day 1, 3 hrs post dose			
n	10	3	13
Mean (SD)	36.78 (4.161)	30.03 (3.800)	35.22 (4.914)
Median	36.25	30.10	33.80
25%, 75%	33.40, 40.00	26.20, 33.80	33.00, 37.10
Min, Max	31.8, 44.2	26.2, 33.8	26.2, 44.2
Day 2, 24 hrs post dose			
n	10	3	13
Mean (SD)	27.23 (3.419)	21.80 (2.066)	25.98 (3.892)
Median	26.25	22.40	26.10
25%, 75%	25.80, 29.40	19.50, 23.50	23.50, 26.30
Min, Max	22.5, 33.1	19.5, 23.5	19.5, 33.1

Notes: All prophylaxis subjects in the PK population were from Israel and had PK assessments collected through Day 10 and all on-demand subjects in the PK population were from Bulgaria and had PK assessments collected through Day 14.
Source: Listing 16.2.6.3
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Time Point	Prophylaxis Treatment (N=10)	On-Demand Treatment (N=3)	Overall Treatment (N=13)
Day 3, 48 hrs post dose			
n	0	3	3
Mean (SD)		16.50 (3.151)	16.50 (3.151)
Median		16.40	16.40
25%, 75%		13.40, 19.70	13.40, 19.70
Min, Max		13.4, 19.7	13.4, 19.7
Day 4, 72 hrs post dose			
n	10	3	13
Mean (SD)	14.83 (1.675)	11.93 (1.041)	14.16 (1.974)
Median	14.55	11.60	14.30
25%, 75%	14.00, 16.40	11.10, 13.10	12.70, 14.70
Min, Max	12.6, 17.7	11.1, 13.1	11.1, 17.7
Day 5, 120 hrs post dose			
n	10	3	13
Mean (SD)	9.52 (1.883)	8.47 (2.354)	9.28 (1.949)
Median	10.20	8.30	10.20
25%, 75%	9.80, 10.60	6.20, 10.90	8.30, 10.60
Min, Max	5.2, 10.9	6.2, 10.9	5.2, 10.9
Day 7, 168 hrs post dose			
n	10	3	13
Mean (SD)	5.54 (1.086)	5.70 (0.755)	5.58 (0.993)
Median	5.60	5.60	5.60
25%, 75%	5.10, 6.20	5.00, 6.50	5.10, 6.20
Min, Max	3.1, 7.2	5.0, 6.5	3.1, 7.2

Notes: All prophylaxis subjects in the PK population were from Israel and had PK assessments collected through Day 10 and all on-demand subjects in the PK population were from Bulgaria and had PK assessments collected through Day 14.
Source: Listing 16.2.6.3
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Time Point	Prophylaxis Treatment (N=10)	On-Demand Treatment (N=3)	Overall Treatment (N=13)
Day 10, 240 hrs post dose			
n	10	3	13
Mean (SD)	3.61 (0.824)	4.80 (1.249)	3.88 (1.020)
Median	3.60	4.40	3.80
25%, 75%	3.00, 4.20	3.80, 6.20	3.40, 4.30
Min, Max	2.1, 5.0	3.8, 6.2	2.1, 6.2
Day 14, 336 hrs post dose			
n	0	3	3
Mean (SD)		2.90 (0.458)	2.90 (0.458)
Median		3.00	3.00
25%, 75%		2.40, 3.30	2.40, 3.30
Min, Max		2.4, 3.3	2.4, 3.3

Notes: All prophylaxis subjects in the PK population were from Israel and had PK assessments collected through Day 10 and all on-demand subjects in the PK population were from Bulgaria and had PK assessments collected through Day 14.
Source: Listing 16.2.6.3
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Source: Study 2004 CSR Table 14.2.6.2

Table A.2-2 Study 2004: Annualized Bleeding Rate by Type of Bleed and Treatment Modality: Treatment Period (Efficacy Population)

Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Spontaneous Bleeding Episodes				
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	7 (53.8)	2 (66.7)	4 (100.0)	11 (64.7)
Number of Subjects with At Least One Post-BL Bleeding Episode Not Requiring Treatment [n (%)]	2 (15.4)	2 (66.7)	0	2 (11.8)
Number of Bleeding Episodes Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	1.1 (1.32)	1.3 (1.53)	8.0 (2.94)	2.7 (3.48)
Median	1.0	1.0	8.0	1.0
25%, 75%	0.0, 2.0	0.0, 3.0	5.5, 10.5	0.0, 4.0
Min, Max	0, 4	0, 3	5, 11	0, 11

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Spontaneous Bleeding Episodes				
Duration of Treatment Period (Days) Per Subject [2]				
n	13	3	4	17
Mean (SD)	314.7 (20.13)	315.0 (24.98)	131.3 (27.50)	271.5 (82.94)
Median	322.0	323.0	132.5	316.0
25%, 75%	315.0, 323.0	287.0, 335.0	107.5, 155.0	259.0, 323.0
Min, Max	259, 335	287, 335	105, 155	105, 335
Annualized Bleeding Rate (Bleeds/Year) Per Subject [3]				
n	13	3	4	17
Mean (SD)	1.255 (1.4967)	1.555 (1.7137)	21.740 (3.9983)	6.075 (9.2142)
Median	1.134	1.273	22.218	1.410
25%, 75%	0.000, 2.269	0.000, 3.392	18.737, 24.743	0.000, 4.523
Min, Max	0.00, 4.52	0.00, 3.39	16.60, 25.92	0.00, 25.92

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Spontaneous Bleeding Episodes				
Annualized Bleeding Rate (Bleeds/Year) [3]				
Total Episodes	14	4	32	46
Total Duration (Years)	11.201	2.587	1.437	12.638
Crude Rate	1.250	1.546	22.263	ND
95% CI	0.683, 2.097	0.421, 3.958	15.228, 31.429	ND, ND
Number of Bleeding Episodes Requiring Treatment Recorded During the Last 12 Weeks of Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.2 (0.38)	0.0 (0.00)	5.5 (1.29)	1.4 (2.43)
Median	0.0	0.0	5.5	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	4.5, 6.5	0.0, 1.0
Min, Max	0, 1	0, 0	4, 7	0, 7

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Spontaneous Bleeding Episodes				
Number of Bleeding Episodes Not Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.2 (0.38)	0.7 (0.58)	0.0 (0.00)	0.1 (0.33)
Median	0.0	1.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 1.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 1	0, 1	0, 0	0, 1

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Traumatic Bleeding Episodes				
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	7 (53.8)	2 (66.7)	2 (50.0)	9 (52.9)
Number of Subjects with At Least One Post-BL Bleeding Episode Not Requiring Treatment [n (%)]	4 (30.8)	1 (33.3)	0	4 (23.5)
Number of Bleeding Episodes Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	2.5 (3.04)	4.7 (5.03)	1.5 (1.91)	2.3 (2.80)
Median	2.0	4.0	1.0	2.0
25%, 75%	0.0, 4.0	0.0, 10.0	0.0, 3.0	0.0, 4.0
Min, Max	0, 10	0, 10	0, 4	0, 10

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Traumatic Bleeding Episodes				
Duration of Treatment Period (Days) Per Subject [2]				
n	13	3	4	17
Mean (SD)	314.7 (20.13)	315.0 (24.98)	131.3 (27.50)	271.5 (82.94)
Median	322.0	323.0	132.5	316.0
25%, 75%	315.0, 323.0	287.0, 335.0	107.5, 155.0	259.0, 323.0
Min, Max	259, 335	287, 335	105, 155	105, 335
Annualized Bleeding Rate (Bleeds/Year) Per Subject [3]				
n	13	3	4	17
Mean (SD)	3.097 (3.8512)	5.750 (6.4513)	5.060 (6.3876)	3.559 (4.4170)
Median	2.255	4.523	3.479	2.255
25%, 75%	0.000, 4.523	0.000, 12.726	0.000, 10.119	0.000, 5.779
Min, Max	0.00, 12.73	0.00, 12.73	0.00, 13.28	0.00, 13.28

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Traumatic Bleeding Episodes				
Annualized Bleeding Rate (Bleeds/Year) [3]				
Total Episodes	33	14	6	39
Total Duration (Years)	11.201	2.587	1.437	12.638
Crude Rate	2.946	5.411	4.174	ND
95% CI	2.028, 4.138	2.958, 9.079	1.532, 9.086	ND, ND
Number of Bleeding Episodes Requiring Treatment Recorded During the Last 12 Weeks of Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.6 (1.19)	1.3 (2.31)	1.3 (1.89)	0.8 (1.35)
Median	0.0	0.0	0.5	0.0
25%, 75%	0.0, 1.0	0.0, 4.0	0.0, 2.5	0.0, 1.0
Min, Max	0, 4	0, 4	0, 4	0, 4

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Traumatic Bleeding Episodes				
Number of Bleeding Episodes Not Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.5 (0.97)	1.0 (1.73)	0.0 (0.00)	0.4 (0.87)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 1.0	0.0, 3.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 3	0, 3	0, 0	0, 3

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Post-Surgery Bleeding Episode				
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	0	0	0	0
Number of Subjects with At Least One Post-BL Bleeding Episode Not Requiring Treatment [n (%)]	0	0	0	0
Number of Bleeding Episodes Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Post-Surgery Bleeding Episode				
Duration of Treatment Period (Days) Per Subject [2]				
n	13	3	4	17
Mean (SD)	314.7 (20.13)	315.0 (24.98)	131.3 (27.50)	271.5 (82.94)
Median	322.0	323.0	132.5	316.0
25%, 75%	315.0, 323.0	287.0, 335.0	107.5, 155.0	259.0, 323.0
Min, Max	259, 335	287, 335	105, 155	105, 335
Annualized Bleeding Rate (Bleeds/Year) Per Subject [3]				
n	13	3	4	17
Mean (SD)	0.000 (0.0000)	0.000 (0.0000)	0.000 (0.0000)	0.000 (0.0000)
Median	0.000	0.000	0.000	0.000
25%, 75%	0.000, 0.000	0.000, 0.000	0.000, 0.000	0.000, 0.000
Min, Max	0.00, 0.00	0.00, 0.00	0.00, 0.00	0.00, 0.00

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Post-Surgery Bleeding Episode				
Annualized Bleeding Rate (Bleeds/Year) [3]				
Total Episodes	0	0	0	0
Total Duration (Years)	11.201	2.587	1.437	12.638
Crude Rate	0.000	0.000	0.000	ND
95% CI	0.000, 0.267	0.000, 1.158	0.000, 2.084	ND, ND
Number of Bleeding Episodes Requiring Treatment Recorded During the Last 12 Weeks of Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Post-Surgery Bleeding Episode				
Number of Bleeding Episodes Not Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Total Bleeding Episodes				
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	8 (61.5)	2 (66.7)	4 (100.0)	12 (70.6)
Number of Subjects with At Least One Post-BL Bleeding Episode Not Requiring Treatment [n (%)]	5 (38.5)	2 (66.7)	0	5 (29.4)
Number of Bleeding Episodes Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	3.6 (3.80)	6.0 (5.57)	9.5 (1.29)	5.0 (4.21)
Median	2.0	7.0	9.5	6.0
25%, 75%	0.0, 7.0	0.0, 11.0	8.5, 10.5	0.0, 8.0
Min, Max	0, 11	0, 11	8, 11	0, 11

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Total Bleeding Episodes				
Duration of Treatment Period (Days) Per Subject [2]				
n	13	3	4	17
Mean (SD)	314.7 (20.13)	315.0 (24.98)	131.3 (27.50)	271.5 (82.94)
Median	322.0	323.0	132.5	316.0
25%, 75%	315.0, 323.0	287.0, 335.0	107.5, 155.0	259.0, 323.0
Min, Max	259, 335	287, 335	105, 155	105, 335
Annualized Bleeding Rate (Bleeds/Year) Per Subject [3]				
n	13	3	4	17
Mean (SD)	4.352 (4.6739)	7.305 (7.0195)	26.800 (2.6963)	9.634 (10.6809)
Median	2.269	7.916	26.875	7.916
25%, 75%	0.000, 8.091	0.000, 13.999	24.743, 28.856	0.000, 13.999
Min, Max	0.00, 14.00	0.00, 14.00	23.56, 29.88	0.00, 29.88

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Total Bleeding Episodes				
Annualized Bleeding Rate (Bleeds/Year) [3]				
Total Episodes	47	18	38	85
Total Duration (Years)	11.201	2.587	1.437	12.638
Crude Rate	4.196	6.957	26.437	ND
95% CI	3.083, 5.580	4.123, 10.995	18.708, 36.287	ND, ND
Number of Bleeding Episodes Requiring Treatment Recorded During the Last 12 Weeks of Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.8 (1.24)	1.3 (2.31)	6.8 (1.26)	2.2 (2.88)
Median	0.0	0.0	7.0	1.0
25%, 75%	0.0, 1.0	0.0, 4.0	6.0, 7.5	0.0, 4.0
Min, Max	0, 4	0, 4	5, 8	0, 8

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	Previous On-Demand Treatment [1] (N=3)	On-Demand Treatment (N=4)	Total (N=17)
Total Bleeding Episodes				
Number of Bleeding Episodes Not Requiring Treatment Per Subject				
n	13	3	4	17
Mean (SD)	0.7 (1.18)	1.7 (2.08)	0.0 (0.00)	0.5 (1.07)
Median	0.0	1.0	0.0	0.0
25%, 75%	0.0, 1.0	0.0, 4.0	0.0, 0.0	0.0, 1.0
Min, Max	0, 4	0, 4	0, 0	0, 4

Note: Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. Percentages are based on the number of subjects in the treatment modality or subpopulation. In this table, Post-BL coincides with Treatment Period. ND denotes Not Done.
[1] Subgroup of subjects in prophylaxis treatment regimen who were receiving on-demand treatment only prior to study entry, as indicated on treatment history form.
[2] Duration of treatment period in days is defined for each subject as the (End of Study Date - Start of Treatment Date + 1).
[3] Annualized Bleeding Rate is calculated as total number of bleeds requiring treatment/(total duration in days from start of treatment period to end of study/365.25). For the crude rate estimate, Annualized Bleeding Rate is calculated by combining total number of bleeds and total duration in years for all subjects in the indicated treatment modality or subpopulation. The 95% confidence interval (one-sided when no events are observed) assumes a Poisson distribution with common underlying intensity and is exact.
Source: Listing 16.2.7.6
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Source: Table 14.2.2.1.

Table A.2-3 Study 2004: Summary of Minor and Moderate Bleeding Episodes by Treatment Modality: Treatment Period (PP Population)

Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Spontaneous Bleeding Episodes			
Number of Subjects with At Least One Post-BL Minor or Moderate Bleeding Episode Requiring Treatment [n (%)]	7 (53.8)	2 (100.0)	9 (60.0)
Location of Bleeding Episode [n (%)]			
Left Ankle	5 (71.4)	1 (50.0)	6 (66.7)
Right Ankle	3 (42.9)	2 (100.0)	5 (55.6)
Left Elbow	2 (28.6)	0	2 (22.2)
Right Elbow	1 (14.3)	1 (50.0)	2 (22.2)
Right Knee	0	2 (100.0)	2 (22.2)
Right Shoulder	0	2 (100.0)	2 (22.2)
Left Foot	0	1 (50.0)	1 (11.1)
Left Forearm	1 (14.3)	0	1 (11.1)
Left Groin	0	1 (50.0)	1 (11.1)
Left Knee	0	1 (50.0)	1 (11.1)
Nasal	1 (14.3)	0	1 (11.1)
Right Groin	0	1 (50.0)	1 (11.1)
Right Hand Back	0	1 (50.0)	1 (11.1)

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Spontaneous Bleeding Episodes			
Total Dose Administered per Episode [1] (IU/kg)			
n	14	21	35
Mean (SD)	66.754 (25.3881)	32.394 (6.1776)	46.138 (23.6763)
Median	64.737	30.510	31.646
25%, 75%	47.426, 74.133	30.221, 31.646	30.316, 59.174
Min, Max	31.17, 125.54	20.74, 47.47	20.74, 125.54

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Traumatic Bleeding Episodes			
Number of Subjects with At Least One Post-BL Minor or Moderate Bleeding Episode Requiring Treatment [n (%)]	7 (53.8)	0	7 (46.7)
Location of Bleeding Episode [n (%)]			
Left Ankle	4 (57.1)	0	4 (57.1)
Right Ankle	3 (42.9)	0	3 (42.9)
Left Knee	2 (28.6)	0	2 (28.6)
Right Hand Front	2 (28.6)	0	2 (28.6)
Right Knee	2 (28.6)	0	2 (28.6)
Left Bicep	1 (14.3)	0	1 (14.3)
Left Elbow	1 (14.3)	0	1 (14.3)
Left Foot	1 (14.3)	0	1 (14.3)
Left Forearm	1 (14.3)	0	1 (14.3)
Left Hand Front	1 (14.3)	0	1 (14.3)
Left Shoulder	1 (14.3)	0	1 (14.3)
Right Bicep	1 (14.3)	0	1 (14.3)
Right Foot	1 (14.3)	0	1 (14.3)
Right Gluteal Muscle (Buttocks)	1 (14.3)	0	1 (14.3)
Right Thigh	1 (14.3)	0	1 (14.3)
Stomach	1 (14.3)	0	1 (14.3)
Other	2 (28.6)	0	2 (28.6)

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
Chiltern • [redacted]20[redacted]:11:48 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_bleed_minor.sas

Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Traumatic Bleeding Episodes			
Total Dose Administered per Episode [1] (IU/kg)			
n	33	0	33
Mean (SD)	66.647 (33.4110)		66.647 (33.4110)
Median	59.174		59.174
25%, 75%	47.783, 73.805		47.783, 73.805
Min, Max	30.79, 151.12		30.79, 151.12

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Post-Surgery Bleeding Episode			
Number of Subjects with At Least One Post-BL Minor or Moderate Bleeding Episode Requiring Treatment [n (%)]	0	0	0
Location of Bleeding Episode [n (%)]			
Total Dose Administered per Episode [1] (IU/kg)			
n	0	0	0
Mean (SD)			
Median			
25%, 75%			
Min, Max			

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Total Bleeding Episodes			
Number of Subjects with At Least One Post-BL Minor or Moderate Bleeding Episode Requiring Treatment [n (%)]	8 (61.5)	2 (100.0)	10 (66.7)
Location of Bleeding Episode [n (%)]			
Left Ankle	5 (62.5)	1 (50.0)	6 (60.0)
Right Ankle	4 (50.0)	2 (100.0)	6 (60.0)
Right Knee	2 (25.0)	2 (100.0)	4 (40.0)
Left Knee	2 (25.0)	1 (50.0)	3 (30.0)
Left Elbow	2 (25.0)	0	2 (20.0)
Left Foot	1 (12.5)	1 (50.0)	2 (20.0)
Left Forearm	2 (25.0)	0	2 (20.0)
Right Elbow	1 (12.5)	1 (50.0)	2 (20.0)
Right Hand Front	2 (25.0)	0	2 (20.0)
Right Shoulder	0	2 (100.0)	2 (20.0)
Left Bicep	1 (12.5)	0	1 (10.0)
Left Groin	0	1 (50.0)	1 (10.0)
Left Hand Front	1 (12.5)	0	1 (10.0)
Left Shoulder	1 (12.5)	0	1 (10.0)
Nasal	1 (12.5)	0	1 (10.0)
Right Bicep	1 (12.5)	0	1 (10.0)
Right Foot	1 (12.5)	0	1 (10.0)
Right Gluteal Muscle (Buttocks)	1 (12.5)	0	1 (10.0)
Right Groin	0	1 (50.0)	1 (10.0)

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Bleeding Type	Prophylaxis Treatment (N=13)	On-Demand Treatment (N=2)	Total (N=15)
Total Bleeding Episodes			
Right Hand Back	0	1 (50.0)	1 (10.0)
Right Thigh	1 (12.5)	0	1 (10.0)
Stomach	1 (12.5)	0	1 (10.0)
Other	2 (25.0)	0	2 (20.0)
Total Dose Administered per Episode [1] (IU/kg)			
n	47	21	68
Mean (SD)	66.679 (30.9631)	32.394 (6.1776)	56.091 (30.4016)
Median	59.174	30.510	48.400
25%, 75%	47.426, 73.805	30.221, 31.646	31.451, 70.174
Min, Max	30.79, 151.12	20.74, 47.47	20.74, 151.12

Note: Percentages for the number of subjects with at least one bleeding episode are based on the number of subjects in the treatment modality. All other counts and percentages are based on the number of subjects with at least one bleeding episode. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. If a subject has multiple bleeding episodes within the same location, the subject is presented only once in the respective subject count [n (%)]. For this table, Post-BL coincides with Treatment Period.
[1] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.7.6
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Source: Study 2004 CSR Table 14.2.3.2.

Table A.2-4 Study 2004: Disease History by Treatment Modality (All Populations)

Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Prophylaxis Treatment (Total)	13 (76.5)	10 (76.9)	13 (76.5)	13 (86.7)
Total Exposure Days (cumulative)				
n	13	10	13	13
Mean (SD)	861.9 (353.61)	954.0 (345.20)	861.9 (353.61)	861.9 (353.61)
Median	750.0	885.0	750.0	750.0
25%, 75%	570.0, 1100.0	700.0, 1300.0	570.0, 1100.0	570.0, 1100.0
Min, Max	415, 1450	520, 1450	415, 1450	415, 1450
Total Exposure Days (within 12 mo)				
n	13	10	13	13
Mean (SD)	80.0 (29.37)	86.0 (26.23)	80.0 (29.37)	80.0 (29.37)
Median	100.0	100.0	100.0	100.0
25%, 75%	50.0, 100.0	50.0, 100.0	50.0, 100.0	50.0, 100.0
Min, Max	30, 110	45, 110	30, 110	30, 110
Bleeds (within 12 mo)				
n	13	10	13	13
Mean (SD)	14.0 (17.97)	8.6 (15.01)	14.0 (17.97)	14.0 (17.97)
Median	6.0	3.0	6.0	6.0
25%, 75%	2.0, 16.0	1.0, 8.0	2.0, 16.0	2.0, 16.0
Min, Max	0, 50	0, 50	0, 50	0, 50

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Spontaneous Bleeds (within 12 mo)				
n	13	10	13	13
Mean (SD)	9.2 (14.73)	5.1 (11.15)	9.2 (14.73)	9.2 (14.73)
Median	1.0	0.0	1.0	1.0
25%, 75%	0.0, 12.0	0.0, 3.0	0.0, 12.0	0.0, 12.0
Min, Max	0, 45	0, 35	0, 45	0, 45
Trauma Induced Bleeds (within 12 mo)				
n	13	10	13	13
Mean (SD)	4.5 (5.21)	3.1 (4.58)	4.5 (5.21)	4.5 (5.21)
Median	3.0	1.5	3.0	3.0
25%, 75%	1.0, 6.0	0.0, 3.0	1.0, 6.0	1.0, 6.0
Min, Max	0, 15	0, 15	0, 15	0, 15
Unknown Bleeds (within 12 mo)				
n	13	10	13	13
Mean (SD)	0.4 (0.87)	0.4 (0.97)	0.4 (0.87)	0.4 (0.87)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 3	0, 3	0, 3	0, 3

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Site of Bleeds [1] [n (%)]				
Muscle/Soft Tissue	5 (38.5)	3 (30.0)	5 (38.5)	5 (38.5)
Mouth/Gums/Nose	1 (7.7)	1 (10.0)	1 (7.7)	1 (7.7)
Hematuria	0	0	0	0
Central Nervous System (CNS)	0	0	0	0
Gastrointestinal (GI)	0	0	0	0
Neck/Throat	0	0	0	0
Severe Trauma Induced Bleeding	0	0	0	0
Joint Bleeding - Knee	4 (30.8)	4 (40.0)	4 (30.8)	4 (30.8)
Joint Bleeding - Elbow	3 (23.1)	3 (30.0)	3 (23.1)	3 (23.1)
Joint Bleeding - Ankle	7 (53.8)	5 (50.0)	7 (53.8)	7 (53.8)
Joint Bleeding - Other (specify)	2 (15.4)	2 (20.0)	2 (15.4)	2 (15.4)
Fingers	1 (7.7)	1 (10.0)	1 (7.7)	1 (7.7)
Thumb,right Middle Fingure	1 (7.7)	1 (10.0)	1 (7.7)	1 (7.7)
Venous Thrombosis	0	0	0	0
Pulmonary Embolism	0	0	0	0
Arterial Thromboses	0	0	0	0
Disseminated Intravascular Coagulation	0	0	0	0
Other (specify)	1 (7.7)	1 (10.0)	1 (7.7)	1 (7.7)
Left Fingure, Right Hand	1 (7.7)	1 (10.0)	1 (7.7)	1 (7.7)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
HIV Status [n (%)]				
Positive	0	0	0	0
Negative	13 (100.0)	10 (100.0)	13 (100.0)	13 (100.0)
HCV Status [n (%)]				
Positive	3 (23.1)	2 (20.0)	3 (23.1)	3 (23.1)
Negative	10 (76.9)	8 (80.0)	10 (76.9)	10 (76.9)
HBV Status [n (%)]				
Positive	0	0	0	0
Negative	13 (100.0)	10 (100.0)	13 (100.0)	13 (100.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Prophylaxis Treatment (Prior On-Demand)	3 (17.6)	1 (7.7)	3 (17.6)	3 (20.0)
Total Exposure Days (cumulative)				
n	3	1	3	3
Mean (SD)	671.7 (373.37)	1100.0	671.7 (373.37)	671.7 (373.37)
Median	500.0	1100.0	500.0	500.0
25%, 75%	415.0, 1100.0	1100.0, 1100.0	415.0, 1100.0	415.0, 1100.0
Min, Max	415, 1100	1100, 1100	415, 1100	415, 1100
Total Exposure Days (within 12 mo)				
n	3	1	3	3
Mean (SD)	43.3 (11.55)	50.0	43.3 (11.55)	43.3 (11.55)
Median	50.0	50.0	50.0	50.0
25%, 75%	30.0, 50.0	50.0, 50.0	30.0, 50.0	30.0, 50.0
Min, Max	30, 50	50, 50	30, 50	30, 50
Bleeds (within 12 mo)				
n	3	1	3	3
Mean (SD)	43.3 (11.55)	50.0	43.3 (11.55)	43.3 (11.55)
Median	50.0	50.0	50.0	50.0
25%, 75%	30.0, 50.0	50.0, 50.0	30.0, 50.0	30.0, 50.0
Min, Max	30, 50	50, 50	30, 50	30, 50

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Spontaneous Bleeds (within 12 mo)				
n	3	1	3	3
Mean (SD)	31.7 (15.28)	35.0	31.7 (15.28)	31.7 (15.28)
Median	35.0	35.0	35.0	35.0
25%, 75%	15.0, 45.0	35.0, 35.0	15.0, 45.0	15.0, 45.0
Min, Max	15, 45	35, 35	15, 45	15, 45
Trauma Induced Bleeds (within 12 mo)				
n	3	1	3	3
Mean (SD)	11.7 (5.77)	15.0	11.7 (5.77)	11.7 (5.77)
Median	15.0	15.0	15.0	15.0
25%, 75%	5.0, 15.0	15.0, 15.0	5.0, 15.0	5.0, 15.0
Min, Max	5, 15	15, 15	5, 15	5, 15
Unknown Bleeds (within 12 mo)				
n	3	1	3	3
Mean (SD)	0.0 (0.00)	0.0	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Site of Bleeds [1] [n (%)]				
Muscle/Soft Tissue	1 (33.3)	0	1 (33.3)	1 (33.3)
Mouth/Gums/Nose	0	0	0	0
Hematuria	0	0	0	0
Central Nervous System (CNS)	0	0	0	0
Gastrointestinal (GI)	0	0	0	0
Neck/Throat	0	0	0	0
Severe Trauma Induced Bleeding	0	0	0	0
Joint Bleeding - Knee	1 (33.3)	1 (100.0)	1 (33.3)	1 (33.3)
Joint Bleeding - Elbow	1 (33.3)	1 (100.0)	1 (33.3)	1 (33.3)
Joint Bleeding - Ankle	3 (100.0)	1 (100.0)	3 (100.0)	3 (100.0)
Joint Bleeding - Other (specify)	1 (33.3)	1 (100.0)	1 (33.3)	1 (33.3)
Fingers	1 (33.3)	1 (100.0)	1 (33.3)	1 (33.3)
Venous Thrombosis	0	0	0	0
Pulmonary Embolism	0	0	0	0
Arterial Thromboses	0	0	0	0
Disseminated Intravascular Coagulation	0	0	0	0
Other (specify)	0	0	0	0
HIV Status [n (%)]				
Positive	0	0	0	0
Negative	3 (100.0)	1 (100.0)	3 (100.0)	3 (100.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
HCV Status [n (%)]				
Positive	1 (33.3)	0	1 (33.3)	1 (33.3)
Negative	2 (66.7)	1 (100.0)	2 (66.7)	2 (66.7)
HBV Status [n (%)]				
Positive	0	0	0	0
Negative	3 (100.0)	1 (100.0)	3 (100.0)	3 (100.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Prophylaxis Treatment (Prior Prophylaxis)	10 (58.8)	9 (69.2)	10 (58.8)	10 (66.7)
Total Exposure Days (cumulative)				
n	10	9	10	10
Mean (SD)	919.0 (346.49)	937.8 (362.07)	919.0 (346.49)	919.0 (346.49)
Median	760.0	770.0	760.0	760.0
25%, 75%	700.0, 1300.0	700.0, 1300.0	700.0, 1300.0	700.0, 1300.0
Min, Max	520, 1450	520, 1450	520, 1450	520, 1450
Total Exposure Days (within 12 mo)				
n	10	9	10	10
Mean (SD)	91.0 (23.19)	90.0 (24.37)	91.0 (23.19)	91.0 (23.19)
Median	100.0	100.0	100.0	100.0
25%, 75%	100.0, 100.0	100.0, 100.0	100.0, 100.0	100.0, 100.0
Min, Max	45, 110	45, 110	45, 110	45, 110
Bleeds (within 12 mo)				
n	10	9	10	10
Mean (SD)	5.2 (5.31)	4.0 (3.94)	5.2 (5.31)	5.2 (5.31)
Median	3.0	3.0	3.0	3.0
25%, 75%	1.0, 8.0	1.0, 6.0	1.0, 8.0	1.0, 8.0
Min, Max	0, 16	0, 12	0, 16	0, 16

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Spontaneous Bleeds (within 12 mo)				
n	10	9	10	10
Mean (SD)	2.4 (4.22)	1.8 (3.96)	2.4 (4.22)	2.4 (4.22)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 3.0	0.0, 1.0	0.0, 3.0	0.0, 3.0
Min, Max	0, 12	0, 12	0, 12	0, 12
Trauma Induced Bleeds (within 12 mo)				
n	10	9	10	10
Mean (SD)	2.3 (2.50)	1.8 (1.99)	2.3 (2.50)	2.3 (2.50)
Median	1.5	1.0	1.5	1.5
25%, 75%	0.0, 3.0	0.0, 3.0	0.0, 3.0	0.0, 3.0
Min, Max	0, 7	0, 6	0, 7	0, 7
Unknown Bleeds (within 12 mo)				
n	10	9	10	10
Mean (SD)	0.5 (0.97)	0.4 (1.01)	0.5 (0.97)	0.5 (0.97)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 1.0	0.0, 0.0	0.0, 1.0	0.0, 1.0
Min, Max	0, 3	0, 3	0, 3	0, 3

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Site of Bleeds [1] [n (%)]				
Muscle/Soft Tissue	4 (40.0)	3 (33.3)	4 (40.0)	4 (40.0)
Mouth/Gums/Nose	1 (10.0)	1 (11.1)	1 (10.0)	1 (10.0)
Hematuria	0	0	0	0
Central Nervous System (CNS)	0	0	0	0
Gastrointestinal (GI)	0	0	0	0
Neck/Throat	0	0	0	0
Severe Trauma Induced Bleeding	0	0	0	0
Joint Bleeding - Knee	3 (30.0)	3 (33.3)	3 (30.0)	3 (30.0)
Joint Bleeding - Elbow	2 (20.0)	2 (22.2)	2 (20.0)	2 (20.0)
Joint Bleeding - Ankle	4 (40.0)	4 (44.4)	4 (40.0)	4 (40.0)
Joint Bleeding - Other (specify)	1 (10.0)	1 (11.1)	1 (10.0)	1 (10.0)
Thumb,right Middle Fingure	1 (10.0)	1 (11.1)	1 (10.0)	1 (10.0)
Venous Thrombosis	0	0	0	0
Pulmonary Embolism	0	0	0	0
Arterial Thromboses	0	0	0	0
Disseminated Intravascular Coagulation	0	0	0	0
Other (specify)	1 (10.0)	1 (11.1)	1 (10.0)	1 (10.0)
Left Fingure, Right Hand	1 (10.0)	1 (11.1)	1 (10.0)	1 (10.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
HIV Status [n (%)]				
Positive	0	0	0	0
Negative	10 (100.0)	9 (100.0)	10 (100.0)	10 (100.0)
HCV Status [n (%)]				
Positive	2 (20.0)	2 (22.2)	2 (20.0)	2 (20.0)
Negative	8 (80.0)	7 (77.8)	8 (80.0)	8 (80.0)
HBV Status [n (%)]				
Positive	0	0	0	0
Negative	10 (100.0)	9 (100.0)	10 (100.0)	10 (100.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
On-Demand Treatment	4 (23.5)	3 (23.1)	4 (23.5)	2 (13.3)
Total Exposure Days (cumulative)				
n	4	3	4	2
Mean (SD)	662.5 (131.50)	600.0 (50.00)	662.5 (131.50)	750.0 (141.42)
Median	625.0	600.0	625.0	750.0
25%, 75%	575.0, 750.0	550.0, 650.0	575.0, 750.0	650.0, 850.0
Min, Max	550, 850	550, 650	550, 850	650, 850
Total Exposure Days (within 12 mo)				
n	4	3	4	2
Mean (SD)	28.8 (2.22)	29.0 (2.65)	28.8 (2.22)	27.0 (1.41)
Median	29.0	30.0	29.0	27.0
25%, 75%	27.0, 30.5	26.0, 31.0	27.0, 30.5	26.0, 28.0
Min, Max	26, 31	26, 31	26, 31	26, 28
Bleeds (within 12 mo)				
n	4	3	4	2
Mean (SD)	27.0 (3.37)	26.7 (4.04)	27.0 (3.37)	27.0 (1.41)
Median	27.0	26.0	27.0	27.0
25%, 75%	24.5, 29.5	23.0, 31.0	24.5, 29.5	26.0, 28.0
Min, Max	23, 31	23, 31	23, 31	26, 28

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Spontaneous Bleeds (within 12 mo)				
n	4	3	4	2
Mean (SD)	27.0 (3.37)	26.7 (4.04)	27.0 (3.37)	27.0 (1.41)
Median	27.0	26.0	27.0	27.0
25%, 75%	24.5, 29.5	23.0, 31.0	24.5, 29.5	26.0, 28.0
Min, Max	23, 31	23, 31	23, 31	26, 28
Trauma Induced Bleeds (within 12 mo)				
n	4	3	4	2
Mean (SD)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0
Unknown Bleeds (within 12 mo)				
n	4	3	4	2
Mean (SD)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Median	0.0	0.0	0.0	0.0
25%, 75%	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Min, Max	0, 0	0, 0	0, 0	0, 0

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Site of Bleeds [1] [n (%)]				
Muscle/Soft Tissue	1 (25.0)	1 (33.3)	1 (25.0)	0
Mouth/Gums/Nose	1 (25.0)	1 (33.3)	1 (25.0)	0
Hematuria	0	0	0	0
Central Nervous System (CNS)	0	0	0	0
Gastrointestinal (GI)	0	0	0	0
Neck/Throat	0	0	0	0
Severe Trauma Induced Bleeding	0	0	0	0
Joint Bleeding - Knee	4 (100.0)	3 (100.0)	4 (100.0)	2 (100.0)
Joint Bleeding - Elbow	4 (100.0)	3 (100.0)	4 (100.0)	2 (100.0)
Joint Bleeding - Ankle	4 (100.0)	3 (100.0)	4 (100.0)	2 (100.0)
Joint Bleeding - Other (specify)	3 (75.0)	3 (100.0)	3 (75.0)	1 (50.0)
Hip Joints - Left And Right	1 (25.0)	1 (33.3)	1 (25.0)	0
Sholder	1 (25.0)	1 (33.3)	1 (25.0)	1 (50.0)
Shoulder	1 (25.0)	1 (33.3)	1 (25.0)	0
Venous Thrombosis	0	0	0	0
Pulmonary Embolism	0	0	0	0
Arterial Thromboses	0	0	0	0
Disseminated Intravascular Coagulation	0	0	0	0
Other (specify)	0	0	0	0

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Treatment Modality	Safety Population (N=17)	PK Population (N=13)	Efficacy Population (N=17)	Per-Protocol Population (N=15)
HIV Status [n (%)]				
Positive	0	0	0	0
Negative	4 (100.0)	3 (100.0)	4 (100.0)	2 (100.0)
HCV Status [n (%)]				
Positive	2 (50.0)	1 (33.3)	2 (50.0)	1 (50.0)
Negative	2 (50.0)	2 (66.7)	2 (50.0)	1 (50.0)
HBV Status [n (%)]				
Positive	1 (25.0)	1 (33.3)	1 (25.0)	1 (50.0)
Negative	3 (75.0)	2 (66.7)	3 (75.0)	1 (50.0)

Note: Percentages for each treatment modality are based on the number of subjects in the population. All other percentages are based the number of subjects receiving each treatment modality.
[1] Site of bleeds within the previous 12 months. Subjects may be counted more than once in location of bleeds and have more than one bleed location.
Source: Listings 16.2.5.6 and 16.2.5.7
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Source: Study 2004 CSR Table 14.1.5.2.

Table A.2-5 Study 2004: Number of rIX-FP Infusions Required to Control Bleeding Episode by Severity: Treatment Period (Efficacy and PP Populations)

Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Minor/Moderate Bleeding Episodes		
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	12 (70.6)	10 (66.7)
Number of Bleeding Episodes Requiring Treatment	85	68
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment	37	22
Number of Bleeding Episodes Requiring Treatment by Subject		
0	5 (29.4)	5 (33.3)
1	0	0
2-3	2 (11.8)	2 (13.3)
4-5	1 (5.9)	1 (6.7)
6-10	7 (41.2)	5 (33.3)
>10	2 (11.8)	2 (13.3)

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Minor/Moderate Bleeding Episodes		
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment by Subject		
0	8 (47.1)	8 (53.3)
1	2 (11.8)	2 (13.3)
2-3	2 (11.8)	2 (13.3)
4-5	2 (11.8)	2 (13.3)
6-10	3 (17.6)	1 (6.7)
>10	0	0
Number of Bleeding Episodes Successfully Managed [1] [n (%)]		
With 1 Infusion	76 (89.4)	60 (88.2)
With 2 Infusions	9 (10.6)	8 (11.8)
With >2 Infusions	0	0

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Minor/Moderate Bleeding Episodes		
Number of Bleeding Episodes Successfully Managed During Last 12 Weeks of Treatment [1] [n (%)]		
With 1 Infusion	35 (94.6)	21 (95.5)
With 2 Infusions	2 (5.4)	1 (4.5)
With >2 Infusions	0	0
Number of Treatments Required to Control Bleeding Episode		
n	85	68
Mean (SD)	1.1 (0.31)	1.1 (0.32)
Median	1.0	1.0
25%, 75%	1.0, 1.0	1.0, 1.0
Min, Max	1, 2	1, 2

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Minor/Moderate Bleeding Episodes		
Number of Maintenance Doses per Bleeding Episode [2]		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		
Total IU Administered per Episode [3]		
n	85	68
Mean (SD)	3597.1 (2356.65)	3932.2 (2479.69)
Median	2874.0	3019.5
25%, 75%	2000.0, 4215.0	2128.0, 4897.0
Min, Max	1313, 13412	1313, 13412

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Minor/Moderate Bleeding Episodes		
Total Dose Administered per Episode [4] (IU/kg)		
n	85	68
Mean (SD)	50.850 (29.4693)	56.091 (30.4016)
Median	45.475	48.400
25%, 75%	30.221, 67.783	31.451, 70.174
Min, Max	19.88, 151.12	20.74, 151.12

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Major Bleeding Episodes		
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	0	0
Number of Bleeding Episodes Requiring Treatment	0	0
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment	0	0
Number of Bleeding Episodes Requiring Treatment by Subject		
0	17 (100.0)	15 (100.0)
1	0	0
2-3	0	0
4-5	0	0
6-10	0	0
>10	0	0

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Major Bleeding Episodes		
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment by Subject		
0	17 (100.0)	15 (100.0)
1	0	0
2-3	0	0
4-5	0	0
6-10	0	0
>10	0	0
Number of Bleeding Episodes Successfully Managed [1] [n (%)]		
With 1 Infusion	0	0
With 2 Infusions	0	0
With >2 Infusions	0	0

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Major Bleeding Episodes		
Number of Bleeding Episodes Successfully Managed During Last 12 Weeks of Treatment [1] [n (%)]		
With 1 Infusion	0	0
With 2 Infusions	0	0
With >2 Infusions	0	0
Number of Treatments Required to Control Bleeding Episode		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Major Bleeding Episodes		
Number of Maintenance Doses per Bleeding Episode [2]		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		
Total IU Administered per Episode [3]		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Major Bleeding Episodes		
Total Dose Administered per Episode [4] (IU/kg)		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Bleeding Episodes		
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment [n (%)]	12 (70.6)	10 (66.7)
Number of Bleeding Episodes Requiring Treatment	85	68
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment	37	22
Number of Bleeding Episodes Requiring Treatment by Subject		
0	5 (29.4)	5 (33.3)
1	0	0
2-3	2 (11.8)	2 (13.3)
4-5	1 (5.9)	1 (6.7)
6-10	7 (41.2)	5 (33.3)
>10	2 (11.8)	2 (13.3)

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Bleeding Episodes		
Number of Bleeding Episodes During Last 12 Weeks of Treatment Requiring Treatment by Subject		
0	8 (47.1)	8 (53.3)
1	2 (11.8)	2 (13.3)
2-3	2 (11.8)	2 (13.3)
4-5	2 (11.8)	2 (13.3)
6-10	3 (17.6)	1 (6.7)
>10	0	0
Number of Bleeding Episodes Successfully Managed [1] [n (%)]		
With 1 Infusion	76 (89.4)	60 (88.2)
With 2 Infusions	9 (10.6)	8 (11.8)
With >2 Infusions	0	0

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
Chiltern • [redacted]20[redacted]11:48 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_bleedinf_sev.sas

Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Bleeding Episodes		
Number of Bleeding Episodes Successfully Managed During Last 12 Weeks of Treatment [1] [n (%)]		
With 1 Infusion	35 (94.6)	21 (95.5)
With 2 Infusions	2 (5.4)	1 (4.5)
With >2 Infusions	0	0
Number of Treatments Required to Control Bleeding Episode		
n	85	68
Mean (SD)	1.1 (0.31)	1.1 (0.32)
Median	1.0	1.0
25%, 75%	1.0, 1.0	1.0, 1.0
Min, Max	1, 2	1, 2

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
Chiltern • [redacted] 11:48 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_bleedinf_sev.sas

Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Bleeding Episodes		
Number of Maintenance Doses per Bleeding Episode [2]		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		
Total IU Administered per Episode [3]		
n	85	68
Mean (SD)	3597.1 (2356.65)	3932.2 (2479.69)
Median	2874.0	3019.5
25%, 75%	2000.0, 4215.0	2128.0, 4897.0
Min, Max	1313, 13412	1313, 13412

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
Chiltern • [redacted] 11:48 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_bleedinf_sev.sas

Bleeding Severity	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Bleeding Episodes		
Total Dose Administered per Episode [4] (IU/kg)		
n	85	68
Mean (SD)	50.850 (29.4693)	56.091 (30.4016)
Median	45.475	48.400
25%, 75%	30.221, 67.783	31.451, 70.174
Min, Max	19.88, 151.12	20.74, 151.12

Note: Percentages for the number of subjects requiring treatment for a bleeding episode are based on the number of subjects in the population. Percentages for bleeding episodes successfully managed are based on the total number of bleeding episodes treated. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. For this table, Post-BL coincides with Treatment Period.
[1] Number of bleeding episodes successfully managed only include infusions needed to achieve hemostasis.
[2] Number of maintenance doses include additional infusions given for a bleed after hemostasis has been achieved.
[3] Total IU administered per bleeding episode sums all doses required to achieve hemostasis for a particular bleeding event.
[4] Total dose administered per bleeding episode (IU/kg) sums all doses required to achieve hemostasis for a particular bleeding event.
Source: Listing 16.2.7.6
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Source: Study 2004 CSR Table 14.2.4.1.

Table A.2-6 Study 2004: Investigator's Clinical Assessment of Hemostatic Efficacy for Treatment of Minor Moderate Bleeding Episodes: Treatment Period (Efficacy and PP Population)

	Efficacy Population (N=17) n (%)	Per-Protocol Population (N=15) n (%)
Number of Subjects with At Least One Post-BL Bleeding Episode Requiring Treatment	12 (70.6)	10 (66.7)
Assessment of Hemostatic Efficacy		
Number of Subjects Assessed	12	10
Number Assessed	85	68
Excellent	53 (62.4)	37 (54.4)
Good	29 (34.1)	28 (41.2)
Moderate	3 (3.5)	3 (4.4)
None	0	0
Assessment of Hemostatic Efficacy During the Last 12 Weeks of Treatment		
Number of Subjects Assessed	9	7
Number Assessed	37	22
Excellent	28 (75.7)	14 (63.6)
Good	8 (21.6)	7 (31.8)
Moderate	1 (2.7)	1 (4.5)
None	0	0

Note: Percentages for number of subjects are based on the number of subjects in the population. Percentages for assessments are based on the number of bleeding episodes assessed. For this table, Post-BL coincides with Treatment Period.
Source: Listing 16.2.7.6
Chiltern • [redacted] 20[redacted] 11:49 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_hemo_minor.sas

	Efficacy Population (N=17) n (%)	Per-Protocol Population (N=15) n (%)
Assessment of Hemostatic Efficacy For Bleeds Treated <4 hrs After Start of Bleed		
Number of Subjects Assessed	11	9
Number Assessed	58	43
Excellent	44 (75.9)	30 (69.8)
Good	14 (24.1)	13 (30.2)
Moderate	0	0
None	0	0
Assessment of Hemostatic Efficacy For Bleeds Treated 4 hrs to <8 hrs After Start of Bleed		
Number of Subjects Assessed	6	5
Number Assessed	13	11
Excellent	5 (38.5)	3 (27.3)
Good	8 (61.5)	8 (72.7)
Moderate	0	0
None	0	0

Note: Percentages for number of subjects are based on the number of subjects in the population. Percentages for assessments are based on the number of bleeding episodes assessed. For this table, Post-BL coincides with Treatment Period.
Source: Listing 16.2.7.6
Chiltern • [redacted] 20[redacted] 11:49 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_hemo_minor.sas

	Efficacy Population (N=17) n (%)	Per-Protocol Population (N=15) n (%)
Assessment of Hemostatic Efficacy For Bleeds Treated 8 hrs to <16 hrs After Start of Bleed		
Number of Subjects Assessed	5	5
Number Assessed	9	9
Excellent	2 (22.2)	2 (22.2)
Good	5 (55.6)	5 (55.6)
Moderate	2 (22.2)	2 (22.2)
None	0	0
Assessment of Hemostatic Efficacy For Bleeds Treated >=16 hrs After Start of Bleed		
Number of Subjects Assessed	2	2
Number Assessed	5	5
Excellent	2 (40.0)	2 (40.0)
Good	2 (40.0)	2 (40.0)
Moderate	1 (20.0)	1 (20.0)
None	0	0

Note: Percentages for number of subjects are based on the number of subjects in the population. Percentages for assessments are based on the number of bleeding episodes assessed. For this table, Post-BL coincides with Treatment Period.
Source: Listing 16.2.7.6
Chiltern • [redacted]20[redacted]11:49 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_hemo_minor.sas

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Source: Study 2004 CSR Table 14.2.4.4.

Table A.2-7 Study 2004: Consumption of rIX-FP During Routine Prophylaxis: Treatment Period (Efficacy and PP Populations)

	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Number of Subjects on Weekly Routine Prophylaxis Treatment [n (%)]	13 (76.5)	13 (86.7)
Number of Subjects Maintaining Weekly Routine Prophylaxis Treatment Through End-of-Study [n (%)] [1]	12 (92.3)	12 (92.3)
Total Number of Prophylaxis Infusions During Study	593	593
Dose Administered per Prophylaxis Infusion (IU/kg)		
n	593	593
Mean (SD)	55.048 (13.8566)	55.048 (13.8566)
Median	50.643	50.643
25%, 75%	48.701, 69.622	48.701, 69.622
Min, Max	15.45, 77.84	15.45, 77.84

Note: Percentages for number of subjects on weekly routine prophylaxis treatment are based on the number of subjects in the population. All other percentages are based on the number of subjects who are on weekly prophylaxis. Only those infusions administered for prophylaxis treatment are included in this summary. In this table, During Study coincides with Treatment Period.
[1] Subjects maintaining weekly routine prophylaxis treatment through end-of-study visit are subjects regarded as compliant with study treatment. Compliance with the weekly prophylaxis regimen is defined as receiving at least 80% of the infusions of rIX-FP at the scheduled infusion frequency (7 days ± 12hrs), unless treatment was interrupted by a bleeding event or surgical procedure.
[2] Summaries per subject per month are calculated for each subject as total number of events or total quantity in treatment period divided by (duration of treatment period in days/(365.25/12)). For summaries per subject per week, denominator is duration of treatment period in days/7. Duration of treatment period in days is defined as the (End of of Study Date - Start of Treatment Period Date + 1).
[3] Dose administered includes each infusion administered for those subjects who maintained a weekly routine prophylaxis regimen through the end-of-study visit, so n is the total number of infusions where data are available.
Source: Listings 16.2.5.1 and 16.2.5.4
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Number of Prophylaxis Infusions per Subject per Month [2]		
n	13	13
Mean (SD)	4.41 (0.052)	4.41 (0.052)
Median	4.43	4.43
25%, 75%	4.35, 4.45	4.35, 4.45
Min, Max	4.3, 4.5	4.3, 4.5
Total Dose Administered per Subject per Month (IU/kg) [2]		
n	13	13
Mean (SD)	243.149 (36.8071)	243.149 (36.8071)
Median	238.403	238.403
25%, 75%	208.285, 278.168	208.285, 278.168
Min, Max	199.24, 303.16	199.24, 303.16

Note: Percentages for number of subjects on weekly routine prophylaxis treatment are based on the number of subjects in the population. All other percentages are based on the number of subjects who are on weekly prophylaxis. Only those infusions administered for prophylaxis treatment are included in this summary. In this table, During Study coincides with Treatment Period.
[1] Subjects maintaining weekly routine prophylaxis treatment through end-of-study visit are subjects regarded as compliant with study treatment. Compliance with the weekly prophylaxis regimen is defined as receiving at least 80% of the infusions of rIX-FP at the scheduled infusion frequency (7 days ± 12hrs), unless treatment was interrupted by a bleeding event or surgical procedure.
[2] Summaries per subject per month are calculated for each subject as total number of events or total quantity in treatment period divided by (duration of treatment period in days/(365.25/12)). For summaries per subject per week, denominator is duration of treatment period in days/7. Duration of treatment period in days is defined as the (End of of Study Date - Start of Treatment Period Date + 1).
[3] Dose administered includes each infusion administered for those subjects who maintained a weekly routine prophylaxis regimen through the end-of-study visit, so n is the total number of infusions where data are available.
Source: Listings 16.2.5.1 and 16.2.5.4
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total Dose Administered per Subject per Week (IU/kg) [2]		
n	13	13
Mean (SD)	55.919 (8.4649)	55.919 (8.4649)
Median	54.828	54.828
25%, 75%	47.901, 63.973	47.901, 63.973
Min, Max	45.82, 69.72	45.82, 69.72
Total IU Administered per Subject per Month [2]		
n	13	13
Mean (SD)	16301.8 (4922.61)	16301.8 (4922.61)
Median	14165.3	14165.3
25%, 75%	12809.1, 17841.0	12809.1, 17841.0
Min, Max	10599, 27418	10599, 27418

Note: Percentages for number of subjects on weekly routine prophylaxis treatment are based on the number of subjects in the population. All other percentages are based on the number of subjects who are on weekly prophylaxis. Only those infusions administered for prophylaxis treatment are included in this summary. In this table, During Study coincides with Treatment Period.
[1] Subjects maintaining weekly routine prophylaxis treatment through end-of-study visit are subjects regarded as compliant with study treatment. Compliance with the weekly prophylaxis regimen is defined as receiving at least 80% of the infusions of rIX-FP at the scheduled infusion frequency (7 days ± 12hrs), unless treatment was interrupted by a bleeding event or surgical procedure.
[2] Summaries per subject per month are calculated for each subject as total number of events or total quantity in treatment period divided by (duration of treatment period in days/(365.25/12)). For summaries per subject per week, denominator is duration of treatment period in days/7. Duration of treatment period in days is defined as the (End of of Study Date - Start of Treatment Period Date + 1).
[3] Dose administered includes each infusion administered for those subjects who maintained a weekly routine prophylaxis regimen through the end-of-study visit, so n is the total number of infusions where data are available.
Source: Listings 16.2.5.1 and 16.2.5.4
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Dose Administered per Infusion for Subjects Maintaining Weekly Routine Prophylaxis Treatment Through End-of-Study [1,3] (IU/kg)		
n	551	551
Mean (SD)	54.842 (13.6141)	54.842 (13.6141)
Median	50.643	50.643
25%, 75%	48.701, 69.420	48.701, 69.420
Min, Max	15.45, 77.84	15.45, 77.84

Note: Percentages for number of subjects on weekly routine prophylaxis treatment are based on the number of subjects in the population. All other percentages are based on the number of subjects who are on weekly prophylaxis. Only those infusions administered for prophylaxis treatment are included in this summary. In this table, During Study coincides with Treatment Period.
[1] Subjects maintaining weekly routine prophylaxis treatment through end-of-study visit are subjects regarded as compliant with study treatment. Compliance with the weekly prophylaxis regimen is defined as receiving at least 80% of the infusions of rIX-FP at the scheduled infusion frequency (7 days ± 12hrs), unless treatment was interrupted by a bleeding event or surgical procedure.
[2] Summaries per subject per month are calculated for each subject as total number of events or total quantity in treatment period divided by (duration of treatment period in days/(365.25/12)). For summaries per subject per week, denominator is duration of treatment period in days/7. Duration of treatment period in days is defined as the (End of of Study Date - Start of Treatment Period Date + 1).
[3] Dose administered includes each infusion administered for those subjects who maintained a weekly routine prophylaxis regimen through the end-of-study visit, so n is the total number of infusions where data are available.
Source: Listings 16.2.5.1 and 16.2.5.4
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Source: Study 2004 CSR Table 14.2.1.1.

Table A.2-8 Study 2004: Dose Assignment and Dose Adjustment by Treatment Modality and Country

	Safety Population (N=17)	Israeli Subjects (N=13)	Bulgarian Subjects (N=4)
Number of Subjects Assigned Prophylaxis Treatment [1]	13 (76.5)	13 (100.0)	0
Inital Dose Assigned (IU/kg)			
n	13	13	0
Mean (SD)	30.35 (3.145)	30.35 (3.145)	
Median	30.00	30.00	
25%, 75%	29.00, 31.00	29.00, 31.00	
Min, Max	25.0, 35.0	25.0, 35.0	
Assigned Infusion Schedule [n (%)]			
Every Week	13 (100.0)	13 (100.0)	0
Every 6 Days	0	0	0
Every 5 Days	0	0	0
Every 4 Days	0	0	0
Other	0	0	0

Note: Percentages for the number of subjects assigned a dose for each treatment modality are based on the number of subjects in the population. Percentages for the assigned infusion schedule and the number of adjustments per subject are based on the number of subjects assigned a dose for that treatment modality. Reason for adjustment percentages are based on the total number of adjustments.
[1] Only subjects assigned to the prophylaxis modality are assigned a prophylaxis dose and infusion schedule. All subjects are assigned an on-demand dose for the treatment of bleeding events. For subjects in the on-demand treatment group, a different on-demand dose may be assigned for joint bleeds and muscle bleeds. The assigned on-demand dose for target joints is summarized.
[2] Total number of adjustments per month may include more than one adjustment per subject.
Source: Listing 16.2.5.2
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	Safety Population (N=17)	Israeli Subjects (N=13)	Bulgarian Subjects (N=4)
Number of Adjustments per Subject [n (%)]			
0	0	0	0
1	2 (15.4)	2 (15.4)	0
2	6 (46.2)	6 (46.2)	0
3	3 (23.1)	3 (23.1)	0
4	0	0	0
5	2 (15.4)	2 (15.4)	0
Number of Adjustments per Month [2]			
Week 1 through 4	0	0	0
Week 5 through 8	12	12	0
Week 9 through 12	5	5	0
Week 13 through 16	4	4	0
Week 17 through 20	5	5	0
Week 21 through 24	5	5	0
Week 25 through 28	1	1	0
Week 29 through 32	1	1	0

Note: Percentages for the number of subjects assigned a dose for each treatment modality are based on the number of subjects in the population. Percentages for the assigned infusion schedule and the number of adjustments per subject are based on the number of subjects assigned a dose for that treatment modality. Reason for adjustment percentages are based on the total number of adjustments.
[1] Only subjects assigned to the prophylaxis modality are assigned a prophylaxis dose and infusion schedule. All subjects are assigned an on-demand dose for the treatment of bleeding events. For subjects in the on-demand treatment group, a different on-demand dose may be assigned for joint bleeds and muscle bleeds. The assigned on-demand dose for target joints is summarized.
[2] Total number of adjustments per month may include more than one adjustment per subject.
Source: Listing 16.2.5.2
Chiltern • [redacted] 20[redacted] 11:49 AM • K:\CSL_Behring\30423\21_Stat\Programs\Tables\t_dose.sas

	Safety Population (N=17)	Israeli Subjects (N=13)	Bulgarian Subjects (N=4)
Reason for Adjustment [n (%)]			
Bleeding	6 (18.2)	6 (18.2)	0
Lack of Efficacy	0	0	0
Physician Decision	23 (69.7)	23 (69.7)	0
Other	4 (12.1)	4 (12.1)	0
Final Dose Assigned (IU/kg)			
n	13	13	0
Mean (SD)	61.92 (11.463)	61.92 (11.463)	
Median	60.00	60.00	
25%, 75%	50.00, 75.00	50.00, 75.00	
Min, Max	50.0, 75.0	50.0, 75.0	
Final Regimen Assigned [n (%)]			
Every Week	13 (100.0)	13 (100.0)	0
Every 6 Days	0	0	0
Every 5 Days	0	0	0
Every 4 Days	0	0	0
Other	0	0	0

Note: Percentages for the number of subjects assigned a dose for each treatment modality are based on the number of subjects in the population. Percentages for the assigned infusion schedule and the number of adjustments per subject are based on the number of subjects assigned a dose for that treatment modality. Reason for adjustment percentages are based on the total number of adjustments.
[1] Only subjects assigned to the prophylaxis modality are assigned a prophylaxis dose and infusion schedule. All subjects are assigned an on-demand dose for the treatment of bleeding events. For subjects in the on-demand treatment group, a different on-demand dose may be assigned for joint bleeds and muscle bleeds. The assigned on-demand dose for target joints is summarized.
[2] Total number of adjustments per month may include more than one adjustment per subject.
Source: Listing 16.2.5.2
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	Safety Population (N=17)	Israeli Subjects (N=13)	Bulgarian Subjects (N=4)
Number of Subjects Assigned On-Demand Treatment [1]	17 (100.0)	13 (100.0)	4 (100.0)
Inital Dose Assigned (IU/kg)			
n	17	13	4
Mean (SD)	33.29 (2.392)	34.31 (1.702)	30.00 (0.000)
Median	35.00	35.00	30.00
25%, 75%	30.00, 35.00	35.00, 35.00	30.00, 30.00
Min, Max	30.0, 35.0	30.0, 35.0	30.0, 30.0
Number of Adjustments per Subject [n (%)]			
0	2 (11.8)	0	2 (50.0)
1	4 (23.5)	3 (23.1)	1 (25.0)
2	5 (29.4)	5 (38.5)	0
3	3 (17.6)	3 (23.1)	0
4	1 (5.9)	0	1 (25.0)
5	2 (11.8)	2 (15.4)	0
Reason for Adjustment [n (%)]			
Bleeding	8 (21.6)	6 (18.8)	2 (40.0)
Lack of Efficacy	0	0	0
Physician Decision	25 (67.6)	22 (68.8)	3 (60.0)
Other	4 (10.8)	4 (12.5)	0

Note: Percentages for the number of subjects assigned a dose for each treatment modality are based on the number of subjects in the population. Percentages for the assigned infusion schedule and the number of adjustments per subject are based on the number of subjects assigned a dose for that treatment modality. Reason for adjustment percentages are based on the total number of adjustments.
[1] Only subjects assigned to the prophylaxis modality are assigned a prophylaxis dose and infusion schedule. All subjects are assigned an on-demand dose for the treatment of bleeding events. For subjects in the on-demand treatment group, a different on-demand dose may be assigned for joint bleeds and muscle bleeds. The assigned on-demand dose for target joints is summarized.
[2] Total number of adjustments per month may include more than one adjustment per subject.
Source: Listing 16.2.5.2
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	Safety Population (N=17)	Israeli Subjects (N=13)	Bulgarian Subjects (N=4)
Final Dose Assigned (IU/kg)			
n	15	13	2
Mean (SD)	57.43 (15.920)	61.92 (11.463)	28.25 (2.475)
Median	55.00	60.00	28.25
25%, 75%	50.00, 75.00	50.00, 75.00	26.50, 30.00
Min, Max	26.5, 75.0	50.0, 75.0	26.5, 30.0

Note: Percentages for the number of subjects assigned a dose for each treatment modality are based on the number of subjects in the population. Percentages for the assigned infusion schedule and the number of adjustments per subject are based on the number of subjects assigned a dose for that treatment modality. Reason for adjustment percentages are based on the total number of adjustments.
[1] Only subjects assigned to the prophylaxis modality are assigned a prophylaxis dose and infusion schedule. All subjects are assigned an on-demand dose for the treatment of bleeding events. For subjects in the on-demand treatment group, a different on-demand dose may be assigned for joint bleeds and muscle bleeds. The assigned on-demand dose for target joints is summarized.
[2] Total number of adjustments per month may include more than one adjustment per subject.
Source: Listing 16.2.5.2
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Source: Study 2004 CSR Table 14.1.9.

Table A.2-9 Study 2004: Consumption of rIX-FP During Surgical Prophylaxis: Treatment Period (Efficacy and PP Population)

	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Number of Subjects Receiving Surgical Prophylaxis [n (%)]	1 (5.9)	1 (6.7)
Total Number of Surgical Prophylaxis Infusions During Study	1	1
Total Number of Surgeries During Study	1	1
Number of Infusions Received per Surgery [n (%)]		
1	1 (100.0)	1 (100.0)

Note: Percentages are based on the number of subjects in the population. All other percentages are based on the number of subjects who received surgical prophylaxis. In this table, During Study coincides with Treatment Period. Subject 40010011 had a mole removed. See Listing 16.2.7.1 for more information.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
Source: Listing 16.2.5.1
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Dose Administered per Infusion(IU/kg) [1]		
Pre-Operation		
n	1	1
Mean (SD)	69.087	69.087
Median	69.087	69.087
25%, 75%	69.087, 69.087	69.087, 69.087
Min, Max	69.09, 69.09	69.09, 69.09
Peri-Operation		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		
Post-Operation		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		

Note: Percentages are based on the number of subjects in the population. All other percentages are based on the number of subjects who received surgical prophylaxis. In this table, During Study coincides with Treatment Period. Subject 40010011 had a mole removed. See Listing 16.2.7.1 for more information.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
Source: Listing 16.2.5.1
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total IU Administered per Infusion		
Pre-Operation		
n	1	1
Mean (SD)	5748.0	5748.0
Median	5748.0	5748.0
25%, 75%	5748.0, 5748.0	5748.0, 5748.0
Min, Max	5748, 5748	5748, 5748
Peri-Operation		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		
Post-Operation		
n	0	0
Mean (SD)		
Median		
25%, 75%		
Min, Max		

Note: Percentages are based on the number of subjects in the population. All other percentages are based on the number of subjects who received surgical prophylaxis. In this table, During Study coincides with Treatment Period. Subject 40010011 had a mole removed. See Listing 16.2.7.1 for more information.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
Source: Listing 16.2.5.1
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Source: Study 2004 CSR Table 14.2.1.3.

Table A.2-10 Study 2004: Derived Efficacy Variables by Subject

Site-Subject Number	Start Date of Trtmnt Period (Time)	Total Number of Bleeding Episodes [1]					Duration of Trtmnt Period (Days) [2]	Annualized Bleeding Rate [3]	Total Dose Per Month (IU/kg) [4]	Total IUs Per Month [4]	Prophylaxis Infusions [4]	Exposure Days [5]
		Requiring Trtmnt	Not Requiring Trtmnt	During Last 12 Weeks	Spontaneous	Traumatic						
40010001	[redacted] (14:00)	7	1	0	4	4	323	7.92	285.63	17841	46	56
40010002	[redacted] (19:55)	8	0	1	4	4	323	9.05	238.40	15607	47	59
40010003	[redacted] (08:40)	0	2	0	0	2	323	0.00	224.80	13455	47	50
40010004	[redacted] (12:10)	0	0	0	0	0	315	0.00	202.12	12809	46	47
40010005	[redacted] (12:21)	2	0	0	2	0	322	2.27	208.28	13878	47	51
40010006	[redacted] (10:51)	4	0	2	1	3	322	4.54	285.30	21042	46	51
40010007	[redacted] (13:34)	11	4	4	2	13	287	14.00	257.24	17377	42	56

NA = Not Applicable
[1] Only bleeding episodes that occurred after dosing on or after the Start Date of Treatment Period are counted. Bleeding Episodes During Last 12 Weeks include only those requiring treatment. Spontaneous and Traumatic Bleeding Episodes include all bleeding episodes regardless of whether treatment was required or not.
[2] Duration of Treatment Period (Days) = (End of Study Date - Start of Treatment Date +1).
[3] Annualized Bleeding Rate = (Number of Bleeding Episodes Requiring Treatment / (Duration of Treatment Period (Days) / 365.25)).
[4] Only doses administered for prophylaxis are included.
[5] Exposure Days includes doses of rIX-FP from this study only. Multiple doses taken on the same day are counted as one exposure day. All doses taken during the study are included.
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Site-Subject Number	Start Date of Trtmnt Period (Time)	Total Number of Bleeding Episodes [1]					Duration of Trtmnt Period (Days) [2]	Annual-ized Bleeding Rate [3]	Total Dose Per Month (IU/kg) [4]	Total IUs Per Month [4]	Prophy-laxis Infusions [4]	Exposure Days [5]
		Requir-ing Trtmnt	Not Requir-ing Trtmnt	During Last 12 Weeks	Spon-taneous	Trau-matic						
40010008	[redacted]20[redacted] (11:52)	6	0	0	1	5	259	8.46	258.23	10599	37	45
40010009	[redacted]20[redacted] (12:26)	0	0	0	0	0	328	0.00	204.66	14165	48	49
40010010	[redacted]20[redacted] (10:27)	0	0	0	0	0	314	0.00	215.69	12028	46	47
40010011	[redacted]20[redacted] (10:30)	0	0	0	0	0	335	0.00	278.17	23068	49	51
40010012	[redacted]20[redacted] (11:10)	2	1	1	0	3	324	2.25	199.24	12637	46	50
40010013	[redacted]20[redacted] (11:55)	7	1	2	2	6	316	8.09	303.16	27418	46	58
50010001	[redacted]20[redacted] (08:47)	10	0	5	10	0	155	23.56	NA	NA	NA	13

NA = Not Applicable
[1] Only bleeding episodes that occurred after dosing on or after the Start Date of Treatment Period are counted. Bleeding Episodes During Last 12 Weeks include only those requiring treatment. Spontaneous and Traumatic Bleeding Episodes include all bleeding episodes regardless of whether treatment was required or not.
[2] Duration of Treatment Period (Days) = (End of Study Date - Start of Treatment Date +1).
[3] Annualized Bleeding Rate = (Number of Bleeding Episodes Requiring Treatment / (Duration of Treatment Period (Days) / 365.25)).
[4] Only doses administered for prophylaxis are included.
[5] Exposure Days includes doses of rIX-FP from this study only. Multiple doses taken on the same day are counted as one exposure day. All doses taken during the study are included.
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Site-Subject Number	Start Date of Trtmnt Period (Time)	Total Number of Bleeding Episodes [1]					Duration of Trtmnt Period (Days) [2]	Annual-ized Bleeding Rate [3]	Total Dose Per Month (IU/kg) [4]	Total IUs Per Month [4]	Prophy-laxis Infusions [4]	Exposure Days [5]
		Requir-ing Trtmnt	Not Requir-ing Trtmnt	During Last 12 Weeks	Spon-taneous	Trau-matic						
50010002	[redacted] (08:30)	11	0	7	11	0	155	25.92	NA	NA	NA	14
50010003	[redacted] (09:21)	9	0	8	5	4	110	29.88	NA	NA	NA	13
50010004	[redacted] (09:50)	8	0	7	6	2	105	27.83	NA	NA	NA	12

NA = Not Applicable
[1] Only bleeding episodes that occurred after dosing on or after the Start Date of Treatment Period are counted. Bleeding Episodes During Last 12 Weeks include only those requiring treatment. Spontaneous and Traumatic Bleeding Episodes include all bleeding episodes regardless of whether treatment was required or not.
[2] Duration of Treatment Period (Days) = (End of Study Date - Start of Treatment Date +1).
[3] Annualized Bleeding Rate = (Number of Bleeding Episodes Requiring Treatment / (Duration of Treatment Period (Days) / 365.25)).
[4] Only doses administered for prophylaxis are included.
[5] Exposure Days includes doses of rIX-FP from this study only. Multiple doses taken on the same day are counted as one exposure day. All doses taken during the study are included.
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Source: Study 2004 CSR Listing 16.2.6.10.

Table A.2-11 Study 2004: Consumption of rIX-FP for the Treatment of Bleeding Episodes: Treatment Period (Efficacy and PP Populations)

	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Number of Subjects Treated for a Bleeding Episode [n (%)]	12 (70.6)	10 (66.7)
Total Number of Infusions for Bleeding Episodes During Study	94	76
Total Number of Bleeding Episodes During Study Requiring Treatment	85	68
Number of Bleeding Episodes During Study Requiring Treatment by Subject		
0	5 (29.4)	5 (33.3)
1	0	0
2-3	2 (11.8)	2 (13.3)
4-5	1 (5.9)	1 (6.7)
6-10	7 (41.2)	5 (33.3)
>10	2 (11.8)	2 (13.3)
Time From the Start of Bleeding Episode to First On-Demand Treatment (hr)		
n	85	68
Mean (SD)	4.554 (7.6976)	5.227 (8.4049)
Median	1.917	2.500
25%, 75%	0.500, 6.333	0.500, 7.000
Min, Max	0.00, 59.03	0.00, 59.03

Note: Percentages are based on the number of subjects in the population. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. In this table, During Study coincides with Treatment Period.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
[2] Dose administered per bleeding episode will sum all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.5.1
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Dose Administered per Infusion(IU/kg) [1]		
n	94	76
Mean (SD)	45.982 (17.9056)	50.187 (17.3492)
Median	39.559	48.400
25%, 75%	30.221, 62.991	31.746, 69.622
Min, Max	19.88, 76.52	20.74, 76.52
Dose Administered per Episode (IU/kg) [2]		
n	85	68
Mean (SD)	50.850 (29.4693)	56.091 (30.4016)
Median	45.475	48.400
25%, 75%	30.221, 67.783	31.451, 70.174
Min, Max	19.88, 151.12	20.74, 151.12
Total IU Administered per Infusion [1]		
n	94	76
Mean (SD)	3252.7 (1491.89)	3518.3 (1525.41)
Median	2874.0	3019.5
25%, 75%	2026.0, 3870.0	2128.0, 4730.0
Min, Max	1313, 7006	1313, 7006

Note: Percentages are based on the number of subjects in the population. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. In this table, During Study coincides with Treatment Period.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
[2] Dose administered per bleeding episode will sum all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.5.1
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	Efficacy Population (N=17)	Per-Protocol Population (N=15)
Total IU Administered per Episode [2]		
n	85	68
Mean (SD)	3597.1 (2356.65)	3932.2 (2479.69)
Median	2874.0	3019.5
25%, 75%	2000.0, 4215.0	2128.0, 4897.0
Min, Max	1313, 13412	1313, 13412

Note: Percentages are based on the number of subjects in the population. Multiple bleeding episodes that occur on the same date/time are counted as a single unique episode with multiple locations. In this table, During Study coincides with Treatment Period.
[1] Dose administered includes each infusion administered, so n is the total number of infusions where data are available.
[2] Dose administered per bleeding episode will sum all doses required to achieve hemostasis for a particular bleeding episode.
Source: Listing 16.2.5.1
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Source: Study 2004 CSR Table 14.2.1.2.

Table A.2-12 Study 2004: Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class Preferred Term	All Subjects (N=17) n (%)	E
Any Treatment-Emergent Adverse Event	14 (82.4)	46
Musculoskeletal and connective tissue disorders	7 (41.2)	17
Arthralgia	5 (29.4)	11
Synovitis	1 (5.9)	2
Bone pain	1 (5.9)	1
Chondropathy	1 (5.9)	1
Joint range of motion decreased	1 (5.9)	1
Muscle spasms	1 (5.9)	1
Injury, poisoning and procedural complications	7 (41.2)	9
Hand fracture	2 (11.8)	2
Laceration	2 (11.8)	2
Contusion	1 (5.9)	1
Head injury	1 (5.9)	1
Injury	1 (5.9)	1
Limb injury	1 (5.9)	1
Radius fracture	1 (5.9)	1
Infections and infestations	4 (23.5)	6
Upper respiratory tract infection	2 (11.8)	4
Pharyngitis	1 (5.9)	1
Tonsillitis	1 (5.9)	1
General disorders and administration site conditions	3 (17.6)	5
Injection site swelling	1 (5.9)	3
Injection site erythema	1 (5.9)	1
Injection site haemorrhage	1 (5.9)	1

Notes: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment.
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System Organ Class Preferred Term	All Subjects (N=17) n (%)	E
Nervous system disorders	4 (23.5)	4
Headache	3 (17.6)	3
Dizziness	1 (5.9)	1
Eye disorders	2 (11.8)	2
Conjunctivitis	1 (5.9)	1
Eye pain	1 (5.9)	1
Gastrointestinal disorders	1 (5.9)	1
Dyspepsia	1 (5.9)	1
Investigations	1 (5.9)	1
Weight decreased	1 (5.9)	1
Skin and subcutaneous tissue disorders	1 (5.9)	1
Rash follicular	1 (5.9)	1

Notes: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment.
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Source: Study 2004 CSR Table 14.3.2.1.

Table A.2-13 Study 2004: Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Relationship to Study Treatment (Safety Population)

System Organ Class Preferred Term Relationship	All Subjects (N=17) n (%)	E
Any Treatment-Emergent Adverse Event	14 (82.4)	46
Not Related	14 (82.4)	46
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Musculoskeletal and connective tissue disorders	7 (41.2)	17
Not Related	7 (41.2)	17
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Arthralgia	5 (29.4)	11
Not Related	5 (29.4)	11
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Synovitis	1 (5.9)	2
Not Related	1 (5.9)	2
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0

Note: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once at the maximum relationship in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related.

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System Organ Class Preferred Term Relationship	All Subjects (N=17) n (%)	E
Bone pain	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Chondropathy	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Joint range of motion decreased	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Muscle spasms	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0

Note: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once at the maximum relationship in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related.

System Organ Class Preferred Term Relationship	All Subjects (N=17) n (%)	E
Injury, poisoning and procedural complications	7 (41.2)	9
Not Related	7 (41.2)	9
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Hand fracture	2 (11.8)	2
Not Related	2 (11.8)	2
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Laceration	2 (11.8)	2
Not Related	2 (11.8)	2
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Contusion	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0

Note: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once at the maximum relationship in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related.

System Organ Class Preferred Term Relationship	All Subjects (N=17) n (%)	E
Head injury	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Injury	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Limb injury	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Radius fracture	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0

Note: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once at the maximum relationship in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related.

System Organ Class Preferred Term Relationship	All Subjects (N=17) n (%)	E
Infections and infestations	4 (23.5)	6
Not Related	4 (23.5)	6
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Upper respiratory tract infection	2 (11.8)	4
Not Related	2 (11.8)	4
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Pharyngitis	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0
Tonsillitis	1 (5.9)	1
Not Related	1 (5.9)	1
Unlikely Related	0	0
Possibly Related	0	0
Probably Related	0	0
Related	0	0

Note: Adverse Events are coded using MedDRA version 15.0. If a subject has multiple occurrences of an AE, the subject is presented only once at the maximum relationship in the respective subject count. Events are counted each time in the event (E) column. Treatment-emergent AEs are defined as AEs that started after the first dose of study treatment. Events with a missing relationship are considered related.