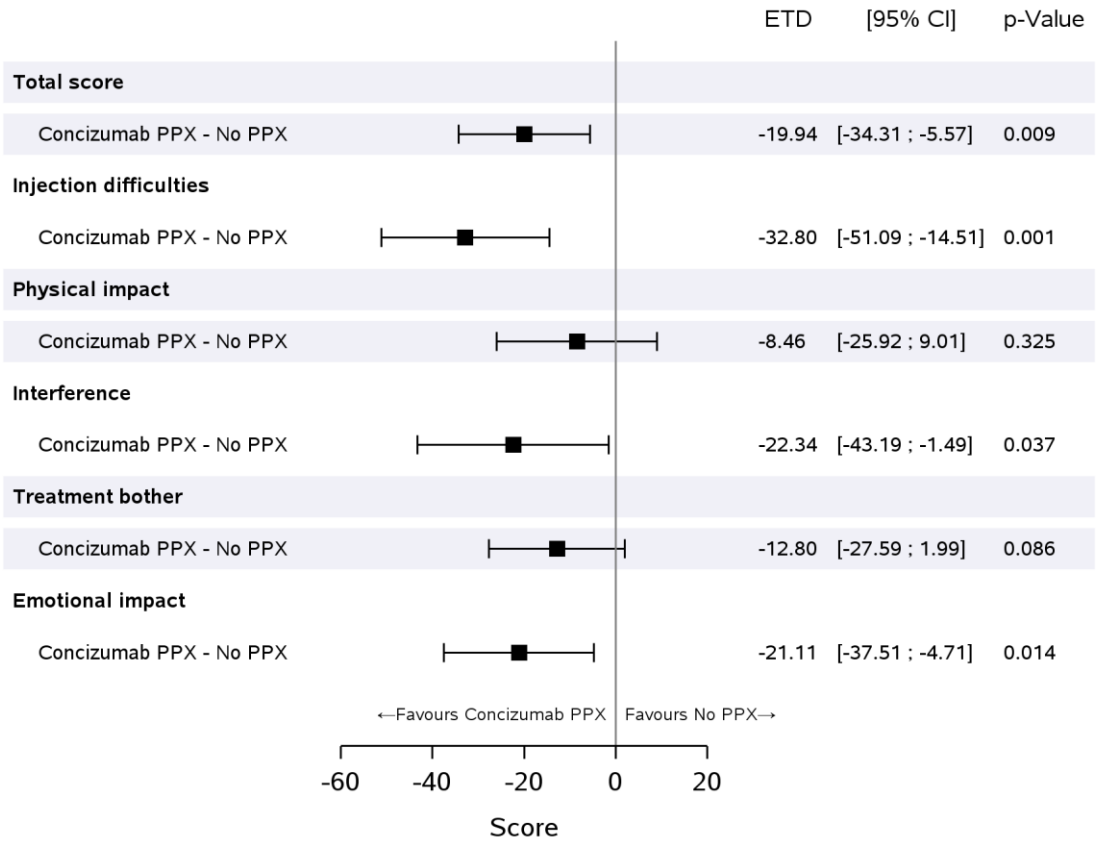
スラインから 24 週までにスコアの平均値の低下が認められたが、その他のドメインのスコアは上昇した〔4311 試験（Module 5.3.5.1）TFL tables 14.2.97～14.2.102〕。

出血時治療（治療群 1）の被験者では平均して 1.0 ポイント悪化したのに対し、コンシズマブによる予防治療を受けた被験者（治療群 2）では Hemo-TEM の総スコアが平均して 16.3 ポイント改善した〔4311 試験（Module 5.3.5.1）TFL Table 14.2.97〕。

事後解析において、Hemo-TEM の総スコアは出血時治療（治療群 1）と比較してコンシズマブによる予防治療（治療群 2）においてベースラインから 24 週にかけて統計的に有意な改善がみられた（図 2.7.3.3-5）。Hemo-TEM の 5 つのすべてのドメインにおいて、出血時治療（治療群 1）と比較してコンシズマブによる予防治療（治療群 2）で好ましい傾向がみられた。総スコア、「注射の困難さ」、「治療による生活への支障」、「治療の精神的影響」においては、統計的に有意な改善がみられた（図 2.7.3.3-5、付録 2.7.3.7.1、Table 114～Table 119）。

図 2.7.3.3-5　血友病治療経験評価（Hemo-TEM）－24 週－フォレストプロット－統計解析－HAwI+HBwI－OTexIR－最大の解析対象集団－4311 試験



HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, ETD: estimated treatment difference, CI: Confidence interval. P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

Hemo-TEM の総スコアにおける 8.0 ポイント以上の改善を臨床的に意味のある被験者内変化の閾値として事前規定した（2.7.3.1.3.8.1 項）。8.0 ポイント以上の改善がみられた被験者をレスポンダーとみなした。

ベースライン及び 24 週両方の質問票の記入を完了した治療群 1 及び 2 の被験者数に基づくと、24 週の Hemo-TEM の総スコアのレスポンダーの割合は、コンシズマブによる予防治療（治療群 2）では 57.9%、出血時治療（治療群 1）では 16.7%であった（付録 2.7.3.7.1、Table 120）。

事後解析において、24 週における Hemo-TEM の総スコアの 8.0 ポイントの改善に関するオッズ（推定値）について、コンシズマブによる予防治療（治療群 2）〔2.6（95%信頼区間：0.55; 12.31）〕と出血時治療（治療群 1）〔0.1（95%信頼区間：0.00; 1.64）〕間で統計的に有意な差がみられた。コンシズマブによる予防治療（治療群 2）と出血時治療（治療群 1）のオッズ比の推定値は 42.55（95%信頼区間：1.05; 1730.79）であった（付録 2.7.3.7.1、Table 121）。

治療の選好性

4311 試験において、被験者の血友病治療の選好性は、被験者に治療の選好性に関する質問を行う Haemophilia Patient Preference Questionnaire（H-PPQ）を用いて 24 週に評価された。

コンシズマブによる予防治療を受け、質問票に回答した被験者（治療群 2～4）83 例のうち、77 例（92.8%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、その主な理由としては出血が少ないこと及び投与の所要時間がより少ないことの 2 つが挙げられていた。5 例が特に好みはないと回答し、1 例がコンシズマブによる予防治療より以前の治療を好むと回答した。16 例は回答しなかった〔4311 試験（Module 5.3.5.1）TFL Table 14.2.103〕。

2.7.3.3.2.1.5　身体活動

4311 試験において、身体活動に関するデータをアクチグラフ社製の小型腕時計タイプの身体活動計を利用して収集した。

コンシズマブによる予防治療（治療群 2）では出血時治療（治療群 1）と比較して中高強度身体活動時間が 1 日の起きている時間あたり 4.4%（推定値、絶対的変化）増加した〔4311 試験（Module 5.3.5.1）Section 11.7〕。例えば平均の起きている時間を 12 時間とすると、4.4%は約 0.5 時間に相当する。

2.7.3.3.2.2　第 2 相試験－臨床的 proof of concept

コンシズマブの第 2 相試験（4310 試験及び 4255 試験）の主要パートの結果から、成人のインヒビターを保有しない血友病 A 患者（4255 試験）及びインヒビターを保有する血友病（4310 試験）におけるコンシズマブの臨床的 proof of concept（CPoC）が確立され、第 3 相試験の 4311 試験及び 4307 試験の開始を支持した。

2 つの第 2 相試験両方において、コンシズマブの曝露量の増加に伴い遊離 TFPI は低下し、トロンビン生成量は正常化した。両方の試験において、プライマリーエンドポイントは年換算の出血率（治療された自然出血及び外傷性出血）であり、主要 CPoC の解析は各被験者において到達した最終の用量レベルでのコンシズマブの効果を評価することを目的として設定し、CPoC は確立された。

4310 試験及び 4255 試験の結果に関する情報の詳細は、各治験総括報告書に示す〔4255 試験 主要パート（Module 5.3.5.2）、4255 試験 延長パート（Module 5.3.5.2）、4310 試験 主要パート（Module 5.3.5.1）及び 4310 試験 延長パート（Module 5.3.5.1）〕。

2.7.3.3.2.3　手術における有効性

2.7.3.3.2.3.1　4311 試験

手術は最大の解析対象集団及び最初の投与方法で投与された期間のデータを除く on-treatment 観察期間（OTexIR）データセットを用いて提示する。

小手術

4311 試験において主要解析の cut-off までに、コンシズマブによる予防治療中（治療群 1 の延長パート及び治療群 2～4）に 7 例が 8 件の小手術を受け、出血時治療（治療群 1 の主要パート）の 1 例が 2 件の小手術を受けた。様々な手術が行われたが、手術に関連する出血エピソードの発現回数は少なく、いずれも軽度／中等度に分類された。小手術によるコンシズマブの治療の変更はなかった。

大手術

4311 試験において、出血時治療（治療群 1）中に 1 例が 1 件の大手術を受けた（クアッドバイクによる事故及び右脛骨開放骨折後の緊急手術）（被験者 ID：[redacted]072）。

2.7.3.3.2.3.2　第 2 相試験－臨床的 proof of concept

小手術

4310 試験においてコンシズマブによる治療中に 6 例が計 16 件の小手術を受け、4255 試験においてはコンシズマブによる治療中に 13 例が計 33 件の小手術を受けた[6]。侵襲性の高い診断のための処置を含む様々な手術が行われたが、手術に関連する出血エピソードの発現回数は少なく、1 回を除きいすれも軽度又は中等度に分類された。手術時には、すべての被験者がコンシズマブ 0.15、0.20 又は 0.25 mg/kg のいずれかの用量の投与を受けていた[6]。第 2 相試験において小手術を受けた 3 件については症例報告において記載されている（植毛[7]、抜歯[7]及びレーザー眼科手術[8]）。

大手術

第 2 相試験において、コンシズマブによる治療中に 1 例が 1 件の大手術を受けた（膝関節置換術[6]、4310 試験 延長パート（Module 5.3.5.1）Appendix 16.2.2、被験者 ID：[redacted]402）。当該大手術に関する詳細は症例報告[9]に示されている。当該大手術に関する詳細情報はノボ ノルディスク社によって収集されていない。

2.7.3.3.3　部分集団における結果の比較

出血時治療と比較したコンシズマブによる予防治療の有効性は、4311 試験（2.7.3.3.2.1 項）において、コンシズマブによる予防治療（治療群 2）と出血時治療（治療群 1）を比較することによって確立された。

さらに、本項では 4311 試験における部分集団におけるコンシズマブによる予防治療の有効性を示す。出血エピソード及び止血薬に関連する結果には治療群 1～4 を用いた。患者報告アウトカム及び身体活動に関連する結果については、これらのデータは試験の主要パートでのみ収集され、治療群 1 の被験者は試験の延長パートでのみコンシズマブの投与を受けたことから、治療群 2～4 を用いた。部分集団間の比較は、主に要約及び記述統計量に基づいている。

部分集団の結果は、4311 試験の主要解析の cut-off までのデータに基づいている。部分集団における結果の提示に用いた解析データセット及び観察期間は、全集団の解析及び結果の提示（2.7.3.3.2.1.1 項及び 2.7.3.3.2.1.4 項）に用いたものと同一とした。

4311 試験におけるコンシズマブの有効性は、年齢グループ別〔青年（12～17 歳）、成人（18 歳以上）〕、血友病の分類別（インヒビターを保有する血友病 A 及びインヒビターを保有する血友病 B）、人種別〔アジア人、黒人／アフリカ系アメリカ人、白人、その他（報告なしを含む）〕、民族別（ヒスパニック／ラテン系又は非ヒスパニック／非ラテン系、報告なし）に探索的に評価された。また、4311 試験におけるコンシズマブの有効性の結果は日本人被験者（2.7.3.3.3.5 項）及び米国人被験者（2.7.3.3.3.6 項）について分けて示す。

2.7.3.3.3.1　年齢グループ別の有効性

4311 試験において、コンシズマブは青年及び成人被験者に対して提供された。主要解析は全集団を対象に行われたが、以下に年齢グループ別の記述統計量の結果を示す。コンパッショネートユースとして主に 12 歳未満のインヒビターを保有する血友病 B 患者に対してコンシズマブを提供した結果については 2.7.3.2.4.2 項及びコンパッショネートユース報告書（Module 5.3.5.4）に示す。

4311 試験において、出血エピソード、止血薬、患者報告アウトカム及び身体活動に対するコンシズマブの有効性は年齢グループ別〔青年（12～17 歳）、成人（18 歳以上）〕に 4311 試験の主要解析の cut-off までのデータに基づいて評価された。

2.7.3.3.3.1.1　出血エピソード

全集団でみられたコンシズマブの効果が、青年又は成人のいずれかでのみみられる効果により得られたことを示す兆候はなかった。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 42 例の青年被験者（治療群 1～4）のうち、主要解析の cut-off までに 20 例（47.6%）が 61 回の治療された出血エピソードを報告した。これらの出血エピソードのうち大部分（52.5%）が自然出血、42.6%が外傷性出血、3.3%が手術によるものであった。出血は関節（82.8%）及び筋肉（6.3%）で高頻度に発現していた（表 2.7.3.3-10）。出血エピソードの大部分（73.8%）が軽度／中等度に分類され、26.2%が重度に分類された。重度の出血は、関節又は標的関節で高頻度に発現しており（付録 2.7.3.7.1、Table 7）、これらの出血の大部分で止血のために必要とされた注射は 1 又は 2 回のみであった（付録 2.7.3.7.1、Table 11）ことから、これらの出血は重度に分類されたものの、コントロールが困難なものではなかった。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 85 例の成人被験者（治療群 1～4）のうち、主要解析の cut-off までに 42 例（49.4%）が 222 回の治療された出血エピソードを報告した。これらの出血エピソードのうち 67.1%が自然出血、32.4%が外傷性出血、0.5%が手術によるものであっ

た。出血は関節（69.2%）及び筋肉（21.5%）で高頻度に発現していた（表 2.7.3.3-10）。出血エピソードの大部分（93.7%）が軽度／中等度に分類され、6.3%が重度に分類された。

表 2.7.3.3-10　治療された出血エピソードー年齢グループ別ー要約ーHAwI+HBwIーOTwoATexIRー最大の解析対象集団ー4311 試験

	Concizumab PPX (arms 1-4)			
	Adolescents		Adults	
	N (%)	E [%]	N (%)	E [%]
N in FAS	42		85	
N in FAS and ADS	42 (100)		85 (100)	
Treated bleeding episodes	20 (47.6)	61 [100]	42 (49.4)	222 [100]
Cause of bleeding episodes				
Spontaneous	16 (38.1)	32 [52.5]	35 (41.2)	149 [67.1]
Traumatic	11 (26.2)	26 [42.6]	28 (32.9)	72 [32.4]
Surgical	1 (2.4)	2 [3.3]	1 (1.2)	1 [0.5]
Missing	1 (2.4)	1 [1.6]	0	
Location of bleeds				
Treated bleeds	20 (47.6)	64 [100]	42 (49.4)	237 [100]
Joint	19 (45.2)	53 [82.8]	34 (40.0)	164 [69.2]
Target joint	8 (19.0)	17 [26.6]	12 (14.1)	61 [25.7]
Muscular	4 (9.5)	4 [6.3]	19 (22.4)	51 [21.5]
Skin	3 (7.1)	3 [4.7]	7 (8.2)	10 [4.2]
Gastrointestinal or Stomach/gut	1 (2.4)	1 [1.6]	1 (1.2)	7 [3.0]
Mouth, gums or nose	2 (4.8)	3 [4.7]	1 (1.2)	1 [0.4]
Urinary system	0		2 (2.4)	2 [0.8]
Central nervous system	0		0	
Other	0		2 (2.4)	2 [0.8]
Classification of bleeding episodes				
Mild/moderate	17 (40.5)	45 [73.8]	40 (47.1)	208 [93.7]
Severe	7 (16.7)	16 [26.2]	11 (12.9)	14 [6.3]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

コンシズマブによる予防治療を受けた全集団（治療群 1～4）における治療された自然出血及び外傷性出血エピソードの年換算の出血率の中央値は 0.0 回／年（2.7.3.3.2.1.1 項）であり、いずれの年齢グループでも同じく 0.0 回／年であった（付録 2.7.3.7.1、Table 8）。

同様に、補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）について、コンシズマブによる予防治療を受けた被験者全体（治療群 1～4）における年換算の出血率の中央値は青年及び成人被験者のいずれにおいても 0.0 回／年であった。すべての治療された及び治療されなかった自然出血及び外傷性出

血エピソードの年換算の出血率の中央値は、青年被験者では 2.6 回／年、成人被験者では 1.8 回／年であった（付録 2.7.3.7.1、Table 8）。

治療された自然出血及び外傷性出血エピソードの年換算の出血率の平均値は青年被験者と成人被験者で大きな違いはなかったものの、コンシズマブによる予防治療を受けた青年被験者と比較して成人被験者でわずかに高かった（付録 2.7.3.7.1、Table 8）。これは主に数例の成人被験者において標的関節のために年換算の出血率が高かった（20 回／年超）ことによるものであった。2 例（被験者 ID：[redacted]075 及び [redacted]071）において被験者の出血の約半分が標的関節で発現しており、1 例（被験者 ID：[redacted]071）では 22 日間しか投与を受けておらず、その間に 3 回の標的関節出血を含む 4 回の出血を報告した（すべて自然出血、年換算の出血率は 66.4 回／年）。

2.7.3.3.3.1.2 止血薬

4311 試験のコンシズマブによる治療の一時中断から再開後（2.7.3.1.2.1 項）、軽度及び中等度の破綻出血の治療ガイダンスが変更された〔4311 試験（Module 5.3.5.1）Appendix 16.1.1 治験実施計画書 Appendix 11〕。

青年及び成人被験者の止血薬の使用量について、1 年あたり、1 回の出血あたり及び 1 回の注射あたりの記述統計量を付録 2.7.3.7.1、Table 9 に示す。出血エピソードあたりの注射回数の要約を付録 2.7.3.7.1、Table 10～Table 12 に示す。止血薬の分類はノボ ノルディスク社の分類に基づく。

2.7.3.3.3.1.3 患者報告アウトカム

患者報告アウトカムからのデータに基づくと、コンシズマブによる予防治療により青年及び成人が異なる影響を受けることを示す兆候はなかった。全体的に、検討した患者報告アウトカムを通じて健康関連の生活の質に関して、いずれの年齢グループにおいても、出血時治療と比較してコンシズマブによる予防治療のほうが好ましい傾向がみられた。いずれの年齢グループにおいても、治療の負担の軽減が認められ、コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者の大部分が、以前の治療よりコンシズマブによる予防治療を好むと回答した。

36-Item Short Form Health Survey（SF-36v2）－年齢グループ別

コンシズマブによる予防治療を受けた被験者（治療群 2～4）のベースラインの平均値は、全体的に成人と比較して青年においてわずかに高かった（付録 2.7.3.7.1、Table 61、Table 63、Table 65、Table 67、Table 69、Table 71、Table 73、Table 75、Table 77 及び Table 79）。

全集団においてみられた SF-36v2 の健康尺度の改善〔4311 試験（Module 5.3.5.1）Section 11.6.1.3〕は、いずれの年齢グループでも保たれていた。コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者ともに、各健康尺度ならびに「身体的側面の QOL サマリースコア」及び「精神的側面の QOL サマリースコア」の平均値はベースラインから 24 週で改善が認められ、これはいずれの年齢グループにおいても機能的健康及びウェルビーイングが改善したことを示していた（表 2.7.3.3-11）。SF-36v2 の青年及び成人被験者の週別の各健康尺度は付録 2.7.3.7.1、Table 61、Table 63、Table 65、Table 67、Table 69、Table 71、Table 73、Table 75、Table 77 及び Table 79 に示す。

表 2.7.3.3-11　SF-36v2－ベースラインから 24 週までの変化量－年齢グループ別－記述統計量－HAwI+HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Change from baseline to week 24 - Bodily pain		
N	24	42
Median	9.9	4.0
P25 ; P75	0.0 ; 16.3	0.0 ; 9.3
Mean (SD)	10.0 (9.8)	5.2 (9.4)
Min ; Max	-4.8 ; 29.8	-13.3 ; 29.0
Change from baseline to week 24 - Physical functioning		
N	24	42
Median	3.8	3.8
P25 ; P75	0.0 ; 7.7	-1.9 ; 7.7
Mean (SD)	3.4 (6.0)	4.5 (7.5)
Min ; Max	-15.3 ; 13.4	-5.8 ; 30.6
Change from baseline to week 24 - Role - Physical		
N	24	42
Median	4.5	4.5
P25 ; P75	0.0 ; 13.5	0.0 ; 11.2
Mean (SD)	5.9 (8.1)	5.3 (10.1)
Min ; Max	-9.0 ; 18.0	-18.0 ; 26.9
Change from baseline to week 24 - General health		
N	24	42
Median	6.2	2.4
P25 ; P75	0.0 ; 12.8	-2.4 ; 10.5
Mean (SD)	8.5 (9.5)	4.2 (10.6)
Min ; Max	-4.8 ; 31.9	-13.3 ; 34.2
Change from baseline to week 24 - Vitality		
N	24	42
Median	5.9	5.9
P25 ; P75	-1.5 ; 10.4	0.0 ; 11.9
Mean (SD)	4.8 (12.2)	7.4 (8.9)
Min ; Max	-26.7 ; 41.6	-5.9 ; 32.7
Change from baseline to week 24 - Social Functioning		
N	24	42
Median	5.0	5.0
P25 ; P75	0.0 ; 10.0	0.0 ; 10.0
Mean (SD)	4.4 (11.6)	6.9 (10.3)
Min ; Max	-15.0 ; 40.1	-10.0 ; 30.1
Change from baseline to week 24 - Role - Emotional		
N	24	42
Median	1.7	0.0
P25 ; P75	0.0 ; 10.5	0.0 ; 10.4
Mean (SD)	4.8 (7.8)	3.8 (10.9)
Min ; Max	-7.0 ; 20.9	-31.3 ; 31.3

Continues on next page

SF-36 v2 – change from baseline to week 24 - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set – trial 4311 - Continued

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
Change from baseline to week 24 – Mental Health		
N	24	42
Median	6.5	1.3
P25 ; P75	-3.9 ; 10.5	-2.6 ; 7.9
Mean (SD)	4.4 (11.3)	4.0 (11.6)
Min ; Max	-15.7 ; 31.4	-13.1 ; 36.6
Change from baseline to week 24 – Physical health component score		
N	24	42
Median	7.5	5.4
P25 ; P75	2.8 ; 11.5	-0.3 ; 10.3
Mean (SD)	7.0 (6.3)	5.0 (8.1)
Min ; Max	-5.4 ; 20.2	-9.6 ; 28.6
Change from baseline to week 24 – Mental health component score		
N	24	42
Median	3.2	3.2
P25 ; P75	-5.3 ; 11.7	-1.7 ; 7.5
Mean (SD)	3.9 (11.3)	5.0 (10.6)
Min ; Max	-12.5 ; 37.9	-11.5 ; 34.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile. Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a－年齢グループ別

全集団においてすべての治療群でみられた PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a により評価された痛みの強度の低下〔4311 試験（Module 5.3.5.1）Section 11.6.2〕は、いずれの年齢グループでも認められた。

コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者のベースラインスコアの平均値は同程度であった（付録 2.7.3.7.1、Table 81）。ベースラインから 24 週でスコアの平均値は青年及び成人被験者ともに低下し、いずれの年齢グループでも痛みの強度が低下したことを示していた。変化量の平均値は、青年で-1.6、成人で-0.8 であった。

PROMIS Short Form v. 2.0 Upper Extremity 7a－年齢グループ別

全集団においてすべてのコンシズマブ治療群でみられた PROMIS Short Form v2.0 Upper Extremity 7a により評価された身体機能の改善〔4311 試験（Module 5.3.5.1）Section 11.6.3〕は、いずれの年齢グループでも認められた。

コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者のベースラインスコアの平均値は同程度であった（付録 2.7.3.7.1、Table 83）。ベースラインから 24 週でスコアの平均値は青年及び成人被験者ともに上昇し、いずれの年齢グループでも身体機能が改善したことを示していた。増加量の平均値は、青年で 4.3、成人で 2.5 であった。

身体機能に関する重症度に対する患者の全般的印象（PGI-S）－年齢グループ別

コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者の週別の重症度に対する患者の全般的印象（PGI-S）の結果の要約を付録 2.7.3.7.1、Table 110 に示す。

青年及び成人被験者ともに、ベースラインと比較して 24 週では「非常に良い」又は「良い」と回答した割合が高く、「悪い」又は「非常に悪い」と回答した割合が低かったことから、より良い身体機能へのシフトが認められた。

ベースラインの身体機能のレベルの回答は、青年では「非常に良い」（14.3%）、「良い」（47.6%）、「まずまず」（33.3%）、「非常に悪い」（4.8%）であり、成人では「非常に良い」（4.9%）、「良い」（26.8%）、「まずまず」（31.7%）、「悪い」（17.1%）、「非常に悪い」（19.5%）であった。

24 週（来院 9／9a）の身体機能のレベルの回答は、青年では「非常に良い」（42.9%）、「良い」（50.0%）、「まずまず」（7.1%）であり、成人では「非常に良い」（18.2%）、「良い」（36.4%）、「まずまず」（36.4%）、「悪い」（9.1%）であった。

身体機能に関する変化に対する患者の全般的印象（PGI-C）－年齢グループ別

コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者の大部分がコンシズマブによる治療を開始後、身体機能が改善したと報告した（付録 2.7.3.7.1、Table 112）。

24 週（来院 9／9a）において、コンシズマブによる治療を開始後、大部分の青年被験者が身体機能に関して「非常に良くなった」（71.4%）又は「まあまあ良くなった」（25.0%）と回答し、3.6%が「変化なし」と回答した。24 週（来院 9／9a）において、大部分の成人被験者が身体機能に関して「非常に良くなった」（47.3%）、「まあまあ良くなった」（30.9%）又は「少し良くなった」（14.5%）と回答し、7.3%が「変化なし」と回答した。

Haemophilia Patient Preference Questionnaire（H-PPQ）－年齢グループ別

24 週の年齢グループ別の治療の選好性に関する質問票（H-PPQ）のデータを付録 2.7.3.7.1、Table 108 に示す。コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人被験者の大部分が以前の治療よりコンシズマブによる予防治療を好むと回答した。

コンシズマブによる予防治療を受け（治療群 2～4）、質問票に回答した青年被験者 28 例のうち、26 例（92.9%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、1 例が好みはないと回答し、1 例がコンシズマブによる予防治療より以前の治療を好むと回答した。6 例は回答しなかった（付録 2.7.3.7.1、Table 108）。

コンシズマブによる予防治療を受け（治療群 2～4）、質問票に回答した成人被験者 55 例のうち、51 例（92.7%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、4 例が好みはないと回答し、コンシズマブによる予防治療より以前の治療を好むと回答した被験者はいなかった。10 例は回答しなかった（付録 2.7.3.7.1、Table 108）。

血友病治療経験評価（Hemo-TEM）－年齢グループ別

コンシズマブによる予防治療群（治療群 2～4）では、ベースラインにおける青年及び成人被験者の Hemo-TEM スコアは全体的に同程度であった（付録 2.7.3.7.1、Table 101～Table 106）。

コンシズマブによる予防治療を受けた（治療群 2～4）青年及び成人いずれの年齢グループにおいても、ベースラインから 24 週までの Hemo-TEM 総スコア及び各ドメインスコアの低下が認められ、治療の負担の軽減が示唆された（表 2.7.3.3-12）。

ベースラインから 24 週までに Hemo-TEM 総スコアは平均して、青年被験者で 14.9 ポイント、成人被験者で 17.7 ポイント改善した（付録 2.7.3.7.1、Table 101）。

週別の Hemo-TEM の各ドメインスコアは青年及び成人被験者別に付録 2.7.3.7.1、Table 101～Table 106 に提示した。

表 2.7.3.3-12　Hemo-TEM－ベースラインから 24 週までの変化量－年齢グループ別－記述統計量－HAwI+HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Change from baseline to week 24 - Total score		
N	21	40
Median	-5.8	-11.1
P25 ; P75	-24.3 ; -2.4	-30.4 ; -0.2
Mean (SD)	-14.9 (22.2)	-17.7 (22.4)
Min ; Max	-81.3 ; 13.2	-68.7 ; 10.5
Change from baseline to week 24 - Injection difficulties		
N	21	40
Median	-8.3	-8.3
P25 ; P75	-41.7 ; 8.3	-29.2 ; 0.0
Mean (SD)	-16.7 (29.9)	-17.9 (30.8)
Min ; Max	-75.0 ; 25.0	-100 ; 50.0
Change from baseline to week 24 - Physical impact		
N	21	40
Median	-8.3	-6.3
P25 ; P75	-33.3 ; 0.0	-20.8 ; 0.0
Mean (SD)	-15.1 (22.9)	-13.6 (20.1)
Min ; Max	-62.5 ; 12.5	-66.7 ; 12.5
Change from baseline to week 24 - Interference		
N	21	40
Median	-6.3	-18.8
P25 ; P75	-31.3 ; 0.0	-39.6 ; 0.0
Mean (SD)	-19.4 (32.6)	-25.4 (30.6)
Min ; Max	-100 ; 18.8	-100 ; 18.8
Change from baseline to week 24 - Treatment bother		
N	21	40
Median	0.0	-14.3
P25 ; P75	-7.1 ; 3.6	-33.9 ; 0.0
Mean (SD)	-7.3 (21.9)	-19.9 (30.9)
Min ; Max	-85.7 ; 25.0	-92.9 ; 85.7
Change from baseline to week 24 - Emotional impact		
N	21	40
Median	-12.5	-4.2
P25 ; P75	-20.8 ; 0.0	-16.7 ; 0.0
Mean (SD)	-16.1 (26.4)	-11.8 (23.9)
Min ; Max	-100 ; 25.0	-83.3 ; 20.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

2.7.3.3.3.1.4　　身体活動

全集団においてみられたコンシズマブによる予防治療（治療群 2 及び 4）におけるベースラインから主要パートの終了時までの 1 日の起きている時間あたりの中高強度身体活動時間（%）の増加〔4311 試験（Module 5.3.5.1）Section 11.7〕は、いずれの年齢グループにおいても認められた。コンシズマブによる予防治療（治療群 2 及び 4）におけるベースラインから主要パートの終了時までの 1 日の起きている時間あたりの中高強度身体活動時間は、青年被験者では 1.3%、成人被験者では 2.0%増加した（付録 2.7.3.7.1、Table 113）。

2.7.3.3.3.2　　血友病の分類別の有効性

主要解析の cut-off までの 4311 試験のデータに基づき、出血エピソード、出血エピソードが起こらなかった被験者の割合（%）、止血薬、患者報告アウトカムに対するコンシズマブの有効性を血友病の分類別（インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者）に評価した。

2.7.3.3.3.2.1　　出血エピソード

出血時治療と比較してコンシズマブによる予防治療はインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者いずれにおいても、年換算の出血率の低下に対して有効であった。

出血パターンはコンシズマブによる予防治療を受けた（治療群 1～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者間で同程度であった（表 2.7.3.3-13）。

76 例のインヒビターを保有する血友病 A 患者のうち、主要解析の cut-off までに 37 例（48.7%）が 129 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（62.8%）であり、35.7%が外傷性出血、0.8%が手術によるものであった。出血エピソードの大部分（85.3%）が軽度／中等度に分類され、14.7%が重度に分類された。これらの出血は関節（76.3%）及び筋肉（15.8%）で高頻度に発現していた。

51 例のインヒビターを保有する血友病 B 患者のうち、主要解析の cut-off までに 25 例（49.0%）が 154 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（64.9%）であり、33.8%が外傷性出血、1.3%が手術によるものであった。出血エピソードの大部分（92.9%）が軽度／中等度に分類され、7.1%が重度に分類された。これらの出血は関節（68.5%）及び筋肉（20.4%）で高頻度に発現していた。

表 2.7.3.3-13　治療された出血エピソードー血友病の分類別ー要約ーHAwI 及び HBwIーOTwoATexIR ー最大の解析対象集団ー4311 試験

	Concizumab(arms 1-4)			
	HAwI		HBwI	
	N (%)	E (%)	N (%)	E (%)
N in FAS	76		51	
N in FAS and ADS	76		51	
Treated bleeding episodes	37 (48.7)	129 [100]	25 (49.0)	154 [100]
Cause of bleeding episodes				
Spontaneous	29 (38.2)	81 [62.8]	22 (43.1)	100 [64.9]
Traumatic	26 (34.2)	46 [35.7]	13 (25.5)	52 [33.8]
Surgical	1 (1.3)	1 [0.8]	1 (2.0)	2 [1.3]
Missing	1 (1.3)	1 [0.8]	0	
Location of bleeds				
Treated bleeds	37 (48.7)	139 [100]	25 (49.0)	162 [100]
Joint	30 (39.5)	106 [76.3]	23 (45.1)	111 [68.5]
Target joint	9 (11.8)	25 [18.0]	11 (21.6)	53 [32.7]
Muscular	15 (19.7)	22 [15.8]	8 (15.7)	33 [20.4]
Skin	6 (7.9)	7 [5.0]	4 (7.8)	6 [3.7]
Gastrointestinal or Stomach/gut	1 (1.3)	1 [0.7]	1 (2.0)	7 [4.3]
Mouth, gums or nose	1 (1.3)	1 [0.7]	2 (3.9)	3 [1.9]
Urinary system	1 (1.3)	1 [0.7]	1 (2.0)	1 [0.6]
Central nervous system	0		0	
Other	1 (1.3)	1 [0.7]	1 (2.0)	1 [0.6]
Classification of bleeding episodes				
Mild/moderate	35 (46.1)	110 [85.3]	22 (43.1)	143 [92.9]
Severe	10 (13.2)	19 [14.7]	8 (15.7)	11 [7.1]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens. N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set. Bleeding episodes with multiple locations are counted in all of these locations.
For location of bleeds and severe bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

プライマリーエンドポイントの治療された自然出血及び外傷性出血エピソードの発現回数については全集団での結果と一致しており、コンシズマブによる予防治療を受けた全集団（治療群 1～4）のインヒビターを保有する血友病 A 患者 76 例及びインヒビターを保有する血友病 B 患者 51 例のいずれにおいても年換算の出血率の中央値は 0.0 回／年であった（付録 2.7.3.7.1、Table 3 及び Table 4）。インヒビターを保有する血友病 A 患者において、年換算の出血率の中央値はコンシズマブによる予防治療（治療群 2）で 1.6 回／年、出血時治療（治療群 1）で 11.8 回／年であった（付録 2.7.3.7.1、Table 3）。インヒビターを保有する血友病 B 患者において、年換算の出血率の中央値はコンシズマブによる予防治療（治療群 2）で 0.0 回／年、出血時治療（治療群 1）で 8.5 回／年であった（付録 2.7.3.7.1、Table 4）。

出血エピソードに関する補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）の年換算の出血率の中央値はプライマリーエンドポイントの結果と一貫していた（付録 2.7.3.7.1、Table 3 及び Table 4）。すべての出血エピソードに関する補足的セカンダリーエンドポイントについて、コンシズマブによる

予防治療を受けた（治療群 1～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者における年換算の出血率の中央値はいずれも 0.0 回／年であった。

コンシズマブによる予防治療を受けた（治療群 1～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者における、すべての治療された及び治療されなかった自然出血及び外傷性出血エピソードに対する年換算の出血率の中央値はいずれも 2.2 回／年であった（付録 2.7.3.7.1、Table 3 及び Table 4）。

インヒビターを保有する血友病 B 患者の稀少性から、インヒビターを保有する血友病 B 患者のみを対象とした優越性の解析は現実的でないと判断された（すなわち、プライマリーエンドポイントは合わせて解析した）。しかし、インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者それぞれに対して統計モデルを当てはめ、血友病の分類別に結果を得たところ、プライマリーエンドポイントの estimand と同じ条件及びストラテジーで検討した場合、治療された自然出血及び外傷性出血エピソードの年換算の出血率の平均の推定値は血友病の分類間で同程度であった。このことから、全集団でプライマリーエンドポイントにおいてみられた効果が、インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者のいずれかの効果によりもたらされたとする兆候は示されなかった（表 2.7.3.3-14）。標的関節により、年換算の出血率（20 回超／年）が高かった 3 例について、1 例はインヒビターを保有する血友病 A 患者（治療群 4）、残り 2 例は、年換算の出血率が 66.4 回／年の 1 例（治療群 2）を含むインヒビターを保有する血友病 B 患者（治療群 2 及び 4）であった（2.7.3.3.3.1.1 項）。

表 2.7.3.3-14　出血エピソード－統計解析－HAwI 及び HBwI－OTwoATexIR－最大の解析対象集団

Population	No PPX (arm 1) Estimated mean ABR [95% CI]	Concizumab PPX (arm2) Estimated mean ABR [95% CI]	ABR ratio [95% CI]
27 HAwI patients	18.3 [10.18; 32.87]	1.6 [0.89; 2.83]	0.09 [0.04; 0.18]
25 HBwI patients	7.2 [2.61; 20.06]	2.2 [0.76; 6.52]	0.31 [0.07; 1.36]

Abbreviations: ABR: annualised bleeding rate, CI: confidence interval, HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: prophylaxis.
Notes: Data is for treated spontaneous and traumatic bleeding episodes.

同様に、出血エピソードに関する補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）及び観察項目であるすべての治療された及び治療されなかった自然出血及び外傷性出血エピソードも、年換算の出血率の平均の推定値はインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者間で同程度であった〔4311 試験（Module 5.3.5.1）TFL Tables 14.2.22 及び 14.2.23〕。

2.7.3.3.3.2.2　治療開始から 24 週間治療された出血エピソードが起こらなかった被験者

いずれの血友病の分類においても、治療開始から 24 週間治療された出血エピソードが起こらなかった被験者の割合は、出血時治療（治療群 1）と比較してコンシズマブ予防治療（治療群 2）で高かった。

コンシズマブによる予防治療を受けたインヒビターを保有する血友病 A 患者 18 例（治療群 2）のうち 9 例（50.0%）で治療開始から 24 週間に治療された自然出血及び外傷性出血エピソードのいずれも

起こらなかった。このうち 8 例（44.4%）が 24 週間の治療を完了し、1 例（5.6%）が 24 週より前に治療を中止していた（表 2.7.3.3-15）。出血時治療（治療群 1）を受けたインヒビターを保有する血友病 A 患者 9 例のうち治療開始から 24 週間に治療された自然出血又は外傷性出血エピソードが起こらなかった被験者はいなかった。

コンシズマブによる予防治療（治療群 2）を受けたインヒビターを保有する血友病 B 患者 15 例のうち 12 例（80.0%）で治療開始から 24 週間に治療された自然出血及び外傷性出血エピソードが起こらなかった。このうち 9 例（60.0%）が 24 週間の治療を完了し、3 例（20.0%）が 24 週より前に治療を中止していた（表 2.7.3.3-15）。出血時治療（治療群 1）を受けたインヒビターを保有する血友病 B 患者 10 例のうち 2 例（20.0%）で治療開始から 24 週間に治療された自然出血及び外傷性出血エピソードが起こらなかった。このうち 1 例（10.0%）が 24 週間の治療を完了し、1 例（10.0%）が 24 週より前に治療を中止していた。

すべての出血に関するエンドポイント及び観察項目について、治療開始から 24 週間にこれらの出血エピソードが起こらなかったインヒビターを保有する血友病 A 患者数及びインヒビターを保有する血友病 B 患者数に関する要約は付録 2.7.3.7.1、Table 5 及び Table 6 に示す。

表 2.7.3.3-15　出血エピソードー治療開始から 24 週間出血エピソードが起こらなかった被験者ー要約ーHAwI 及び HBwIーOTwoATexIRー最大の解析対象集団ー4311 試験

	No PPX	Concizumab PPX			
	(Arm 1) N (%)	(Arm 2) N (%)	(Arm 3) N (%)	(Arm 4) N (%)	(Arms 2-4) N (%)
HAwI					
N in FAS	9	18	13	40	71
N in FAS and ADS	9(100)	18(100)	13(100)	40(100)	71(100)
Zero Treated spontaneous and traumatic bleeds					
Yes	0	9(50.0)	9(69.2)	26(65.0)	44(62.0)
Yes, and completed 24 weeks	0	8(44.4)	4(30.8)	23(57.5)	35(49.3)
Yes, but discontinued before 24 weeks	0	1(5.6)	5(38.5)	3(7.5)	9(12.7)
No	9(100.0)	9(50.0)	4(30.8)	14(35.0)	27(38.0)
HBwI					
N in FAS	10	15	8	20	43
N in FAS and ADS	10(100)	15(100)	8(100)	20(100)	43(100)
Zero Treated spontaneous and traumatic bleeds					
Yes	2(20.0)	12(80.0)	3(37.5)	9(45.0)	24(55.8)
Yes, and completed 24 weeks	1(10.0)	9(60.0)	3(37.5)	7(35.0)	19(44.2)
Yes, but discontinued before 24 weeks	1(10.0)	3(20.0)	0	2(10.0)	5(11.6)
No	8(80.0)	3(20.0)	5(62.5)	11(55.0)	19(44.2)

HAwI: haemophilia A with inhibitors, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

2.7.3.3.3.2.3　　止血薬

4311 試験のコンシズマブによる治療の一時中断から再開後（2.7.3.1.2.1 項）、軽度及び中等度の破綻出血の治療ガイダンスが変更された〔4311 試験（Module 5.3.5.1）Appendix 16.1.1 治験実施計画書 Appendix 11〕。

インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の止血薬の使用量について、1 年あたり、1 回の出血あたり及び 1 回の注射あたりの記述統計量を治験総括報告書〔4311 試験（Module 5.3.5.1）TFL Tables 14.2.34 及び 14.2.35〕に示す。インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の出血エピソードあたりの注射回数の要約を治験総括報告書〔4311 試験（Module 5.3.5.1）TFL Tables 14.2.36～14.2.38〕に示す。止血薬の分類はノボ ノルディスク社の分類に基づく。

2.7.3.3.3.2.4　　患者報告アウトカム

検討した患者報告アウトカムを通じて健康関連の生活の質に関して、いずれの血友病の分類においても、出血時治療と比較してコンシズマブによる予防治療のほうが好ましい傾向がみられた。全体的に、インヒビターを保有する血友病 A 患者と比較してインヒビターを保有する血友病 B 患者においてより顕著な改善がみられた。いずれの血友病の分類においても、治療の負担の軽減が認められ、コンシズマブによる予防治療を受けたインヒビターを保有する血友病 A 患者とインヒビターを保有する血友病 B 患者（治療群 2～4）はともに大部分の被験者が、以前の治療よりコンシズマブによる予防治療を好むと回答した。

36-Item Short Form Health Survey（SF-36v2）－血友病の分類別

コンシズマブによる予防治療を受けた被験者（治療群 2～4）のベースラインの平均値は、全体的にインヒビターを保有する血友病 B 患者（HBwI）と比較してインヒビターを保有する血友病 A 患者（HAwI）において高く、インヒビターを保有する血友病 A 患者においてベースラインの生活の質はより高かったことを示していた（付録 2.7.3.7.1、Table 60、Table 62、Table 64、Table 66、Table 68、Table 70、Table 72、Table 74、Table 76 及び Table 78）。

全集団（HAwI+HBwI）においてみられた SF-36v2 の健康尺度の改善〔4311 試験（Module 5.3.5.1）Section 11.6.1.3〕は、いずれの血友病の分類でも保たれていた。コンシズマブによる予防治療を受けた（治療群 2～4）インヒビターを保有する血友病 A 患者とインヒビターを保有する血友病 B 患者ともに、各健康尺度ならびに「身体的側面の QOL サマリースコア」及び「精神的側面の QOL サマリースコア」の平均値はベースラインから 24 週で改善が認められ、これはいずれの血友病の分類においても機能的健康及びウェルビーイングが改善したことを示していた（表 2.7.3.3-16）。すべての健康尺度及びサマリースコアにおいて、インヒビターを保有する血友病 A 患者と比較してインヒビターを保有する血友病 B 患者においてより顕著な改善がみられた。インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の週別の SF-36v2 の健康尺度の記述統計量は付録 2.7.3.7.1、Table 60、Table 62、Table 64、Table 66、Table 68、Table 70、Table 72、Table 74、Table 76 及び Table 78 に示す。

表 2.7.3.3-16　SF-36v2－ベースラインから 24 週までの変化量－血友病の分類別－記述統計量－HAwI 及び HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Change from baseline to week 24 - Bodily pain		
N	41	25
Median	4.8	6.5
P25 ; P75	0.0 ; 12.5	0.0 ; 10.5
Mean (SD)	6.9 (9.7)	7.0 (10.1)
Min ; Max	-13.3 ; 27.8	-13.3 ; 29.8
Change from baseline to week 24 - Physical functioning		
N	41	25
Median	3.8	3.8
P25 ; P75	0.0 ; 7.7	0.0 ; 7.7
Mean (SD)	3.4 (6.3)	5.4 (7.8)
Min ; Max	-15.3 ; 17.2	-3.8 ; 30.6
Change from baseline to week 24 - Role - Physical		
N	41	25
Median	4.5	4.5
P25 ; P75	0.0 ; 13.5	2.3 ; 11.2
Mean (SD)	4.7 (9.8)	6.8 (8.7)
Min ; Max	-18.0 ; 22.5	-9.0 ; 26.9
Change from baseline to week 24 - General Health		
N	41	25
Median	3.8	4.8
P25 ; P75	0.0 ; 10.5	0.0 ; 12.8
Mean (SD)	5.5 (9.6)	6.2 (11.7)
Min ; Max	-12.8 ; 31.9	-13.3 ; 34.2
Change from baseline to week 24 - Vitality		
N	41	25
Median	5.9	5.9
P25 ; P75	0.0 ; 11.9	0.0 ; 11.9
Mean (SD)	5.7 (9.0)	7.8 (12.1)
Min ; Max	-26.7 ; 20.8	-8.9 ; 41.6
Change from baseline to week 24 - Social Functioning		
N	41	25
Median	5.0	5.0
P25 ; P75	0.0 ; 10.0	0.0 ; 10.0
Mean (SD)	4.9 (9.9)	7.8 (12.0)
Min ; Max	-15.0 ; 30.1	-10.0 ; 40.1
Change from baseline to week 24 - Role - Emotional		
N	41	25
Median	0.0	3.5
P25 ; P75	-3.5 ; 7.0	0.0 ; 10.5
Mean (SD)	3.2 (11.2)	5.7 (6.8)
Min ; Max	-31.3 ; 31.3	-3.5 ; 24.4

Continues on next page

SF-36 v2 - change from baseline to week 24 - by haemophilia subtype - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311 - Continued

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
Change from baseline to week 24 - Mental Health		
N	41	25
Median	2.6	2.6
P25 ; P75	-2.6 ; 10.5	-2.6 ; 10.5
Mean (SD)	4.0 (10.6)	4.5 (12.8)
Min ; Max	-13.1 ; 28.8	-15.7 ; 36.6
Change from baseline to week 24 - Physical health component score		
N	41	25
Median	5.3	6.3
P25 ; P75	0.4 ; 10.3	1.7 ; 10.3
Mean (SD)	5.3 (6.8)	6.5 (8.6)
Min ; Max	-9.2 ; 18.1	-9.6 ; 28.6
Change from baseline to week 24 - Mental health component score		
N	41	25
Median	1.9	3.6
P25 ; P75	-2.4 ; 8.5	-0.4 ; 9.9
Mean (SD)	3.9 (10.4)	5.8 (11.5)
Min ; Max	-12.5 ; 34.0	-10.8 ; 37.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a－血友病の分類別

全集団においてすべての治療群でみられた PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a により評価された痛みの強度の低下〔4311 試験（Module 5.3.5.1）Section 11.6.2〕は、いずれの血友病の分類でも認められた。

コンシズマブによる予防治療を受けた被験者（治療群 2～4）において、ベースラインスコアの平均値は血友病の分類を通じて同程度であった（付録 2.7.3.7.1、Table 80）。ベースラインから 24 週でスコアの平均値はインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者ともに低下し、いずれの血友病の分類でも痛みの強度が低下したことを示していた。変化量の平均値は、インヒビターを保有する血友病 A 患者で-1.4、インヒビターを保有する血友病 B 患者で-0.5 であった。

PROMIS Short Form v. 2.0 Upper Extremity 7a－血友病の分類別

全集団においてすべての治療群でみられた PROMIS Short Form v2.0 Upper Extremity 7a により評価された身体機能の改善〔4311 試験（Module 5.3.5.1）Section 11.6.3〕は、いずれの血友病の分類でも認められた。

コンシズマブによる予防治療を受けた被験者（治療群 2～4）において、ベースラインスコアの平均値は血友病の分類を通じて同程度であった（付録 2.7.3.7.1、Table 82）。ベースラインから 24 週でスコアの平均値はインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者ともに

上昇し、いずれの血友病の分類でも身体機能が改善したことを示していた。増加量の平均値は、インヒビターを保有する血友病 A 患者で 3.0、インヒビターを保有する血友病 B 患者で 3.6 であった。

成人血友病患者用 QOL 質問票（Haem-A-QoL）－血友病の分類別

全集団においてみられた生活の質の改善〔4311 試験（Module 5.3.5.1）Section 11.6.4〕は、いずれの血友病の分類でも認められた。

コンシズマブによる予防治療を受けた被験者（治療群 2～4）において、Haem-A-QoL のベースラインの平均値は、全体的にインヒビターを保有する血友病 B 患者と比較してインヒビターを保有する血友病 A 患者において低く、インヒビターを保有する血友病 A 患者においてベースラインの生活の質が良かったことを示していた（付録 2.7.3.7.1、Table 84～Table 94）。

コンシズマブによる予防治療を受けたインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者（治療群 2～4）において、ベースラインから 24 週までにドメインスコアの低下が認められ、インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者ともに健康に関する生活の質が改善したことを示していた（表 2.7.3.3-17）。すべてのドメインにおいて、インヒビターを保有する血友病 A 患者と比較してインヒビターを保有する血友病 B 患者においてより顕著な改善がみられた（表 2.7.3.3-17）。

ベースラインから 24 週までに Haem-A-QoL の総スコアは平均して、インヒビターを保有する血友病 A 患者で 9.7 ポイント、インヒビターを保有する血友病 B 患者で 18.7 ポイント改善した。

表 2.7.3.3-17　成人血友病患者用 QOL 質問票（Haem-A-QoL）（17 歳以上）－ベースラインから 24 週までの変化量－血友病の分類別－記述統計量－HAwI 及び HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Change from baseline to week 24 - Total Score		
N	25	14
Median	-6.8	-17.3
P25 ; P75	-16.2 ; -2.4	-30.4 ; -0.7
Mean (SD)	-9.7 (18.2)	-18.7 (20.8)
Min ; Max	-51.1 ; 43.0	-57.9 ; 7.0
Change from baseline to week 24 - Physical health		
N	25	14
Median	-15.0	-32.5
P25 ; P75	-30.0 ; -2.5	-45.0 ; -10.0
Mean (SD)	-10.8 (32.3)	-33.9 (24.2)
Min ; Max	-50.0 ; 95.0	-75.0 ; 0.0
Change from baseline to week 24 - Feeling		
N	25	14
Median	-12.5	-18.8
P25 ; P75	-25.0 ; 0.0	-37.5 ; 0.0
Mean (SD)	-13.0 (25.6)	-21.4 (29.6)
Min ; Max	-68.8 ; 56.3	-87.5 ; 12.5
Change from baseline to week 24 - View of yourself		
N	24	14
Median	0.0	-17.5
P25 ; P75	-20.0 ; 12.5	-35.0 ; 0.0
Mean (SD)	-3.8 (20.4)	-19.6 (22.3)
Min ; Max	-55.0 ; 30.0	-70.0 ; 5.0
Change from baseline to week 24 - Sport and leisure		
N	18	9
Median	-4.4	-15.0
P25 ; P75	-15.0 ; 0.0	-45.0 ; -5.0
Mean (SD)	-11.9 (19.7)	-20.7 (22.3)
Min ; Max	-62.5 ; 6.3	-48.8 ; 10.0
Change from baseline to week 24 - Work and studies		
N	22	7
Median	-6.3	-18.8
P25 ; P75	-25.0 ; 6.3	-50.0 ; -6.3
Mean (SD)	-13.9 (24.8)	-25.3 (21.8)
Min ; Max	-68.8 ; 25.0	-56.3 ; 0.0
Change from baseline to week 24 - Dealing with haemophilia		
N	25	14
Median	0.0	-8.3
P25 ; P75	-8.3 ; 16.7	-16.7 ; 0.0
Mean (SD)	-0.7 (23.6)	-12.5 (27.5)
Min ; Max	-50.0 ; 41.7	-100 ; 16.7

Continues on next page

Haemophilia quality of life questionnaire for adults (Haem-A-QoL) >= 17 years - change from baseline to week 24 - by haemophilia subtype - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311 - Continued

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
Change from baseline to week 24 - Treatment		
N	24	14
Median	-12.5	-17.2
P25 ; P75	-31.3 ; -4.7	-31.3 ; 0.0
Mean (SD)	-16.3 (27.4)	-17.9 (23.3)
Min ; Max	-87.5 ; 56.3	-59.4 ; 18.8
Change from baseline to week 24 - Future		
N	24	14
Median	-7.5	-10.0
P25 ; P75	-17.5 ; 0.0	-40.0 ; 10.0
Mean (SD)	-8.9 (23.2)	-15.4 (28.8)
Min ; Max	-70.0 ; 55.0	-70.0 ; 20.0
Change from baseline to week 24 - Family planning		
N	12	8
Median	0.0	-16.7
P25 ; P75	-18.8 ; 3.1	-41.7 ; 6.3
Mean (SD)	-6.6 (16.1)	-15.4 (30.1)
Min ; Max	-37.5 ; 14.6	-50.0 ; 31.3
Change from baseline to week 24 - Partnership and sexuality		
N	25	14
Median	0.0	0.0
P25 ; P75	-25.0 ; 8.3	-16.7 ; 8.3
Mean (SD)	-4.0 (21.4)	-7.7 (39.6)
Min ; Max	-41.7 ; 50.0	-83.3 ; 50.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

身体機能に関する重症度に対する患者の全般的印象（PGI-S）－血友病の分類別

コンシズマブによる予防治療を受けた（治療群 2～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の週別の PGI-S の結果の要約を付録 2.7.3.7.1、Table 109 に示す。

インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者において、ベースラインと比較して 24 週では「非常に良い」又は「良い」と回答した割合が高く、「悪い」又は「非常に悪い」と回答した割合が低かったことから、いずれの血友病の分類においても、より良い身体機能へのシフトが認められた。

ベースラインの身体機能のレベルの回答は、インヒビターを保有する血友病 A 患者では「非常に良い」（10.5%）、「良い」（39.5%）、「まずまず」（26.3%）、「悪い」（13.2%）、「非常に悪い」（10.5%）であり、インヒビターを保有する血友病 B 患者では「非常に良い」（4.2%）、「良い」（25.0%）、「まずまず」（41.7%）、「悪い」（8.3%）、「非常に悪い」（20.8）であった（付録 2.7.3.7.1、Table 109）。

24 週（来院 9／9a）の身体機能のレベルの回答は、インヒビターを保有する血友病 A 患者では「非常に良い」（30.8%）、「良い」（34.6%）、「まずまず」（28.8%）、「悪い」（5.8%）であり、インヒビターを保有する血友病 B 患者では「非常に良い」（19.4%）、「良い」（51.6%）、「まずまず」（22.6%）、「悪い」（6.5%）であった（付録 2.7.3.7.1、Table 109）。

身体機能に関する変化に対する患者の全般的印象（PGI-C）－血友病の分類別

コンシズマブによる予防治療を受けた（治療群 2～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の大部分がコンシズマブによる治療を開始後、身体機能が改善したと報告した（付録 2.7.3.7.1、Table 111）。

24 週（来院 9／9a）において、コンシズマブによる治療を開始後、インヒビターを保有する血友病 A 患者の多くが身体機能に関して「非常に良くなった」（50.0%）、「まあまあ良くなった」（34.6%）又は「少し良くなった」（9.6%）と回答し、5.8%が「変化なし」と回答した。24 週（来院 9／9a）において、インヒビターを保有する血友病 B 患者の多くが身体機能に関して「非常に良くなった」（64.5%）、「まあまあ良くなった」（19.4%）又は「少し良くなった」（9.7%）と回答し、6.5%が「変化なし」と回答した。

Haemophilia Patient Preference Questionnaire（H-PPQ）－血友病の分類別

24 週の血友病の分類別の治療の選好性に関する質問票（H-PPQ）のデータを付録 2.7.3.7.1、Table 107 に示す。コンシズマブによる予防治療を受けたインヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者（治療群 2～4）の大部分が以前の治療よりコンシズマブによる予防治療を好むと回答した。

コンシズマブによる予防治療を受け（治療群 2～4）、質問票に回答したインヒビターを保有する血友病 A 患者の 52 例のうち、47 例（90.4%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、4 例が特に好みはないと回答し、1 例がコンシズマブによる予防治療より以前の治療を好むと回答した。10 例は回答しなかった（付録 2.7.3.7.1、Table 107）。

コンシズマブによる予防治療を受け、質問票に回答したインヒビターを保有する血友病 B 患者（治療群 2～4）の 31 例のうち、30 例（96.8%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、1 例が特に好みはないと回答し、コンシズマブによる予防治療より以前の治療を好むと回答した被験者はいなかった。6 例は回答しなかった（付録 2.7.3.7.1、Table 107）。

血友病治療経験評価（Hemo-TEM）－血友病の分類別

コンシズマブによる予防治療を受けた被験者（治療群 2～4）では、ベースラインにおける Hemo-TEM スコアはインヒビターを保有する血友病 B 患者と比較してインヒビターを保有する血友病 A 患者において低く、インヒビターを保有する血友病 A 患者においてベースラインの治療の負担が少ないことが示された。

コンシズマブによる予防治療を受けた（治療群 2～4）インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者のいずれも、ベースラインから 24 週までの Hemo-TEM 総スコア及び各ドメインスコアの低下が認められ、治療の負担の軽減が示された（表 2.7.3.3-18）。すべてのド

メインにおいて、インヒビターを保有する血友病 A 患者と比較してインヒビターを保有する血友病 B 患者において改善はわずかに大きかった。

ベースラインから 24 週までに Hemo-TEM 総スコアは平均して、インヒビターを保有する血友病 A 患者では 15.2 ポイント、インヒビターを保有する血友病 B 患者では 19.4 ポイント改善した（付録 2.7.3.7.1、Table 95）。

インヒビターを保有する血友病 A 患者及びインヒビターを保有する血友病 B 患者の週別の Hemo-TEM の各ドメインの結果を付録 2.7.3.7.1、Table 95～Table 100 に示す。

表 2.7.3.3-18　Hemo-TEM－ベースラインから 24 週までの変化量－血友病の分類別－記述統計量－HAwI 及び HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Change from baseline to week 24 - Total Score		
N	38	23
Median	-10.2	-10.0
P25 ; P75	-25.5 ; -0.7	-45.2 ; 0.5
Mean (SD)	-15.2 (18.6)	-19.4 (27.4)
Min ; Max	-67.3 ; 13.2	-81.3 ; 10.5
Change from baseline to week 24 - Injection difficulties		
N	38	23
Median	-8.3	-8.3
P25 ; P75	-25.0 ; 0.0	-41.7 ; 0.0
Mean (SD)	-14.9 (31.2)	-21.7 (28.7)
Min ; Max	-100 ; 50.0	-83.3 ; 25.0
Change from baseline to week 24 - Physical Impact		
N	38	23
Median	-6.3	-8.3
P25 ; P75	-20.8 ; 4.2	-41.7 ; 0.0
Mean (SD)	-12.0 (19.6)	-17.8 (22.9)
Min ; Max	-66.7 ; 12.5	-62.5 ; 8.3
Change from baseline to week 24 - Interference		
N	38	23
Median	-18.8	-12.5
P25 ; P75	-37.5 ; 0.0	-50.0 ; 0.0
Mean (SD)	-22.1 (26.8)	-25.4 (37.9)
Min ; Max	-93.8 ; 18.8	-100 ; 18.8
Change from baseline to week 24 - Treatment bother		
N	38	23
Median	-8.9	-7.1
P25 ; P75	-28.6 ; 0.0	-35.7 ; 0.0
Mean (SD)	-14.5 (22.8)	-17.4 (36.8)
Min ; Max	-82.1 ; 25.0	-92.9 ; 85.77
Change from baseline to week 24 - Emotional impact		
N	38	23
Median	-8.3	0.0
P25 ; P75	-16.7 ; 0.0	-41.7 ; 4.2
Mean (SD)	-12.4 (19.2)	-14.7 (32.2)
Min ; Max	-70.8 ; 25.0	-100 ; 20.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

2.7.3.3.3.3　人種別の有効性

主要解析の cut-off までの 4311 試験のデータに基づき、コンシズマブの出血エピソードに対する有効性を人種別〔アジア人、黒人／アフリカ系アメリカ人、白人又はその他（「アメリカ先住民又はアラスカ先住民」及び「報告なし」）〕に評価した。

2.7.3.3.3.3.1　出血エピソード

全集団でみられた年換算の出血率に対するコンシズマブの効果が特定の人種でのみみられる効果により得られたことは示唆されなかった。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 34 例のアジア人被験者（治療群 1～4）のうち、主要解析の cut-off までに 22 例（64.7%）が 79 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（67.1%）であり、32.9%が外傷性出血であった。これらの出血は関節（72.3%）及び筋肉（14.5%）で高頻度に発現していた。出血エピソードの多く（73.4%）が軽度／中等度に分類され、26.6%が重度に分類された（表 2.7.3.3-19）。重度の出血は、関節又は標的関節で高頻度に発現していた（付録 2.7.3.7.1、Table 13）。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 9 例の黒人／アフリカ系アメリカ人被験者（治療群 1～4）のうち、主要解析の cut-off までに 4 例（44.4%）が 9 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（55.6%）であり、33.3%が外傷性出血〔1 回（11.1%）の原因は不明〕であった。9 回のすべて出血エピソード（100%）が軽度／中等度に分類され、すべて（100%）が関節に発現していた（表 2.7.3.3-19）。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 76 例の白人被験者（治療群 1～4）のうち、主要解析の cut-off までに 36 例（47.4%）が 195 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（63.1%）であり、35.4%が外傷性出血であった。出血エピソードの大部分（95.4%）が軽度／中等度に分類され、4.6%が重度に分類された。出血は関節（70.4%）及び筋肉（20.9%）で高頻度に発現していた（表 2.7.3.3-19）。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 8 例のその他に分類された被験者（治療群 1～4）からは治療された出血エピソード報告の報告はなかった。

プライマリーエンドポイントの治療された自然出血及び外傷性出血エピソードの発現回数について、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、アジア人では 1.5 回／年、黒人／アフリカ系アメリカ人、白人及びその他の人種では 0.0 回／年であった（付録 2.7.3.7.1、Table 14）。出血エピソードに関する補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）の年換算の出血率の中央値はプライマリーエンドポイントの結果と一貫していた（付録 2.7.3.7.1、Table 14）。すべての治療された及び治療されなかった自然出血及び外傷性出血エピソードついて、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、アジア人では 3.6 回／年、黒人／アフリカ系アメリカ人では 1.9 回／年、白人では 1.9 回／年、及びその他の人種では 0.8 回／年であった（付録 2.7.3.7.1、Table 14）。

表 2.7.3.3-19　治療された出血エピソードー人種別ー要約ーHAwI+HBwIーOTwoATexIRー最大の解析対象集団ー4311 試験

	Concizumab PPX (arms 1-4)							
	Asian		Black or African American		White		Other	
	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]
N in FAS	34		9		76		8	
N in FAS and ADS	34 (100)		9 (100)		76 (100)		8 (100)	
Treated bleeding episodes	22 (64.7)	79 [100]	4 (44.4)	9 [100]	36 (47.4)	195 [100]	0	
Cause of bleeding episodes								
Spontaneous	18 (52.9)	53 [67.1]	3 (33.3)	5 [55.6]	30 (39.5)	123 [63.1]	0	
Traumatic	12 (35.3)	26 [32.9]	2 (22.2)	3 [33.3]	25 (32.9)	69 [35.4]	0	
Surgical	0		0		2 (2.6)	3 [1.5]	0	
Missing	0		1 (11.1)	1 [11.1]	0		0	
Location of bleeds								
Treated bleeds	22 (64.7)	83 [100]	4 (44.4)	12 [100]	36 (47.4)	206 [100]	0	
Joint	18 (52.9)	60 [72.3]	4 (44.4)	12 [100]	31 (40.8)	145 [70.4]	0	
Target joint	6 (17.6)	16 [19.3]	1 (11.1)	1 [8.3]	13 (17.1)	61 [29.6]	0	
Muscular	9 (26.5)	12 [14.5]	0		14 (18.4)	43 [20.9]	0	
Skin	1 (2.9)	1 [1.2]	0		9 (11.8)	12 [5.8]	0	
Gastrointestinal or Stomach/gut	2 (5.9)	8 [9.6]	0		0		0	
Mouth, gums or nose	1 (2.9)	1 [1.2]	0		2 (2.6)	3 [1.5]	0	
Urinary system	1 (2.9)	1 [1.2]	0		1 (1.3)	1 [0.5]	0	
Central nervous system	0		0		0		0	
Other	0		0		2 (2.6)	2 [1.0]	0	
Classification of bleeding episodes								
Mild/moderate	20 (58.8)	58 [73.4]	4 (44.4)	9 [100]	33 (43.4)	186 [95.4]	0	
Severe	11 (32.4)	21 [26.6]	0		7 (9.2)	9 [4.6]	0	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
Other race includes 'American Indian or Alaska Native' and 'Not Reported'.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

2.7.3.3.3.4　民族別の有効性

主要解析の cut-off までの 4311 試験のデータに基づき、コンシズマブの出血エピソードに対する有効性を民族別（非ヒスパニック／非ラテン系、ヒスパニック／ラテン系又は「報告なし」）に評価した。ヒスパニック／ラテン系の被験者は 6 例、報告なしの被験者は 4 例と少ないことから、これらの民族の部分集団における結果の解釈は注意する必要がある。

2.7.3.3.3.4.1　出血エピソード

全集団でみられた年換算の出血率に対するコンシズマブの効果が特定の民族でのみみられる効果により得られたことを示す兆候はなかった。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 117 例の非ヒスパニック／非ラテン系被験者（治療群 1～4）のうち、主要解析の cut-off までに 62 例（53.0%）が 283 回の治療された出血エピソードを報告した。これらの出血エピソードの多くが自然出血（64.0%）であり、34.6%が外傷性出血、1.1%が手術によるものであった〔1 回（0.4%）の出血の原因は不明〕。出血エピソードの多く（89.4%）が軽度／中等度に分類され、10.6%が重度に分類された。出血は関節（72.1%）及び筋肉（18.3%）で高頻度に発現していた（表 2.7.3.3-20）。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた（治療群 1～4）ヒスパニック／ラテン系被験者 6 例及び民族が「報告されていない」被験者 4 例からは、主要解析の cut-off までに治療された出血エピソードの報告はなかった（表 2.7.3.3-20）。

プライマリーエンドポイントの治療された自然出血及び外傷性出血エピソードの発現回数について、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、非ヒスパニック／非ラテン系被験者では 0.9 回／年、ヒスパニック／ラテン系被験者及び民族が「報告されていない」被験者では 0.0 回／年であった（付録 2.7.3.7.1、Table 16）。出血エピソードに関する 3 つの補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）について、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、いずれの民族においても 0.0 回／年であった（付録 2.7.3.7.1、Table 16）。すべての治療された及び治療されなかった自然出血及び外傷性出血エピソードについて、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、非ヒスパニック／非ラテン系被験者では 2.3 回／年、ヒスパニック／ラテン系被験者では 1.3 回／年、及び民族が「報告されていない」被験者では 0.0 回／年であった（付録 2.7.3.7.1、Table 16）。

表 2.7.3.3-20　治療された出血エピソードー民族別ー要約ーHAwI+HBwIーOTwoATexIRー最大の解析対象集団ー4311 試験

	Concizumab PPX (arms 1-4)		
	Hispanic or Latino N (%) E [%]	Not Hispanic or Latino N (%) E [%]	Not Reported N (%) E [%]
N in FAS	6	117	4
N in FAS and ADS	6 (100)	117 (100)	4 (100)
Treated bleeding episodes	0	62 (53.0) 283 [100]	0
Cause of bleeding episodes			
Spontaneous	0	51 (43.6) 181 [64.0]	0
Traumatic	0	39 (33.3) 98 [34.6]	0
Surgical	0	2 (1.7) 3 [1.1]	0
Missing	0	1 (0.9) 1 [0.4]	0
Location of bleeds			
Treated bleeds	0	62 (53.0) 301 [100]	0
Joint	0	53 (45.3) 217 [72.1]	0
Target joint	0	20 (17.1) 78 [25.9]	0
Muscular	0	23 (19.7) 55 [18.3]	0
Skin	0	10 (8.5) 13 [4.3]	0
Gastrointestinal or Stomach/gut	0	2 (1.7) 8 [2.7]	0
Mouth, gums or nose	0	3 (2.6) 4 [1.3]	0
Urinary system	0	2 (1.7) 2 [0.7]	0
Central nervous system	0	0	0
Other	0	2 (1.7) 2 [0.7]	0
Classification of bleeding episodes			
Mild/moderate	0	57 (48.7) 253 [89.4]	0
Severe	0	18 (15.4) 30 [10.6]	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

2.7.3.3.3.5　日本人における有効性

4311 試験

計 7 例の日本人被験者がスクリーニングを受けた（2.7.3.3.1.1.1.1 項）。人口統計学的特性及びベースライン特性について、日本人集団と全集団間で明らかな違いは認められなかった（2.7.3.3.1.1.2.1 項）。

治療群 1 の 1 例の被験者は延長パートには参加せず、治療群 4 の 1 例が治療の一時中断後に再開しなかったため、5 例の日本人被験者がコンシズマブの維持用量の設定を行った。このうち 4 例が用量を 0.20 mg/kg に維持し、1 例が維持用量を 0.25 mg/kg に設定した（付録 2.7.3.7.1、Table 59）。

日本人被験者の出血エピソードの一覧を付録 2.7.3.7.1、Table 123 に示す。日本人被験者 7 例の年換算の出血率の記述統計量を付録 2.7.3.7.1、Table 53 に示す。被験者数が少ないことから、結果の解釈は注意する必要がある。プライマリーエンドポイントの治療された自然出血及び外傷性出血エピソードの発現回数について、治療の一時中断前及び後（OTwoATexIR 解析データセット）にコンシズマブによる予防治療を受けた日本人被験者 6 例（治療群 2～4）の年換算の出血率の中央値は、3.0 回／年であった。コンシズマブによる予防治療を受けた 1 例（治療群 2）の年換算の出血率は 16.8 回／年であり、出血時治療（非予防治療）を行った 1 例（治療群 1）の年換算の出血率は 3.2 回／年であった。治療群 2 の被験者（被験者 ID：[redacted]071）は、4322 試験から移行した被験者であり、前治療は出血時治療であった。4322 試験における年換算の出血率は 49.4 回／年であった〔4322 試験（Module 5.3.5.4）Listing 16.2.5.4、被験者 ID：NN7415-4322/[redacted]001〕。したがって、当該被験者ではコンシズマブによる治療開始後に臨床的に意味のある年換算の出血率の低下がみられ、4311 試験（被験者 ID：[redacted]071）において当該被験者が 1 年以上コンシズマブの投与を受けたという事実は、コンシズマブによる治療のベネフィットを示唆している。当該被験者については、2 つの標的関節（左右の肘）が報告され、4311 試験に参加した時点で血友病性関節症を合併していた。

出血エピソードに関する補足的セカンダリーエンドポイント（治療された自然出血ならびに治療された自然発症及び外傷性の関節出血）の年換算の出血率の中央値は、プライマリーエンドポイントの結果と一貫していた。コンシズマブによる予防治療を受けた日本人被験者 6 例（治療群 2～4）において、出血エピソードに関する補足的セカンダリーエンドポイントの治療された自然発症及び外傷性の標的関節出血の年換算の出血率の中央値は 0.0 回／年であった。コンシズマブによる予防治療を受けた 1 例（治療群 2）の年換算の出血率は 3.7 回／年であり、出血時治療（非予防治療）を行った 1 例（治療群 1）の年換算の出血率は 0.0 回／年であった。

コンシズマブによる予防治療を受けた被験者 6 例（治療群 2～4）における、すべての治療された及び治療されなかった自然出血及び外傷性出血エピソードに対する年換算の出血率の中央値は 7.5 回／年であった。コンシズマブによる予防治療を受けた 1 例（治療群 2）の年換算の出血率は 17.7 回／年、出血時治療（非予防治療）を行った 1 例（治療群 1）の年換算の出血率は 3.2 回／年であった。

コンシズマブによる予防治療を受けた日本人被験者 6 例の年換算の出血率を血友病の分類及び年齢グループ別に付録 2.7.3.7.1、Table 54 及び Table 55 に示す。

4311 試験の日本人被験者と全集団との間で、図 2.7.3.1-4 及び 2.7.3.4 項に示した投与方法でコンシズマブを投与したときの有効性に差があることを示す兆候はなかった。プライマリーエンドポイントについて、日本人のコンシズマブによる予防治療を受けた被験者 1 例の年換算の出血率が 16.8 回／年で

あったことは留意する必要があるが、これは 1 件の観察値で予想外のものではなく、当該被験者の前治療における年換算の出血率が 49.4 回／年であったことと比較すると、臨床的に意義のある改善がみられたと考えられる。

第 2 相試験

2 つの第 2 相試験に 6 例の日本人被験者が組み入れられ、4255 試験にインヒビターを保有しない血友病 A 患者 4 例〔4255 試験 主要パート（Module 5.3.5.2）TFL Table 14.2.2〕、4310 試験にインヒビターを保有する血友病患者 2 例〔4310 試験 主要パート（Module 5.3.5.1）TFL Table 14.2.2〕が組み入れられた。

人口統計学的特性及びベースライン特性について、日本人集団と非日本人集団で全体的に同様であり、2 つの第 2 相試験〔4255 試験 主要パート（Module 5.3.5.2）及び 4310 試験 主要パート（Module 5.3.5.1）〕の主要パートにおいて日本人被験者における有効性データは非日本人集団と同程度であった。

2.7.3.3.3.6　米国人における有効性

米国人における出血エピソード、止血薬及び患者報告アウトカムに対するコンシズマブの有効性は 4311 試験の主要解析の cut-off までのデータを用いて、米国人対非米国人の比較に基づいて評価された。

2.7.3.3.3.6.1　出血エピソード

4311 試験において米国人と非米国人の間で出血エピソードに違いがあることは示唆されなかった。米国人及び非米国人におけるすべての治療された出血エピソードの要約を付録 2.7.3.7.1、Table 17 に示す。

治療の一時中断前及び後にコンシズマブによる予防治療を受けた 6 例の米国人被験者（治療群 1～4）のうち、主要解析の cut-off までに 1 例（16.7%）が 4 回の出血エピソードを報告した。4 回の出血エピソードすべて（100%）が自然出血であり、軽度／中等度に分類された。すべての出血が関節で発現していた。

米国人及び非米国人被験者の出血に関するすべてのエンドポイントの年換算の出血率及び観察項目の記述統計量を付録 2.7.3.7.1、Table 18 に示す。

プライマリーエンドポイントの治療された自然出血及び外傷性出血エピソードの年換算の出血率の中央値は、コンシズマブによる予防治療を受けた米国人被験者（治療群 1～4）では 0.0 回／年、非米国人では 0.8 回／年であった（付録 2.7.3.7.1、Table 18）。

出血エピソードに関する補足的セカンダリーエンドポイント（治療された自然出血、治療された自然発症及び外傷性の関節出血、治療された自然発症及び外傷性の標的関節出血）の年換算の出血率の中央値は、コンシズマブによる予防治療を受けた米国人被験者及び非米国人被験者（治療群 1～4）いずれも 0.0 回／年であり、プライマリーエンドポイントの結果と一貫していた（付録 2.7.3.7.1、Table 18）。

すべての治療された及び治療されなかった自然出血及び外傷性出血エピソードついて、コンシズマブによる予防治療を受けた被験者（治療群 1～4）の年換算の出血率の中央値は、米国人被験者では 0.0 回／年、非米国人被験者では 2.2 回／年であった（付録 2.7.3.7.1、Table 18）。

2.7.3.3.3.6.2　　止血薬

4311 試験のコンシズマブによる治療の一時中断から再開後（2.7.3.1.2.1 項）、軽度及び中等度の破綻出血の治療ガイダンスが変更された〔4311 試験（Module 5.3.5.1）Appendix 16.1.1 治験実施計画書 Appendix 11〕。

米国人及び非米国人被験者の止血薬の使用量について、1 年あたり、1 回の出血あたり及び 1 回の注射あたりの記述統計量を付録 2.7.3.7.1、Table 19 に示す。出血エピソードあたりの注射回数の要約を付録 2.7.3.7.1、Table 20 に示す。止血薬の分類はノボ ノルディスク社の分類に基づく。

2.7.3.3.3.6.3　　患者報告アウトカム

患者報告アウトカムからの結果に基づくと、米国人及び非米国人被験者でコンシズマブによる予防治療に対する反応が異なったことを示す兆候はなかった。全体的に、検討した患者報告アウトカムを通じて健康関連の生活の質に関して、米国人及び非米国人被験者のいずれでも、出血時治療と比較してコンシズマブによる予防治療で好ましい傾向がみられた。いずれのグループにおいても、治療の負担の軽減が認められ、コンシズマブによる予防治療を受けた（治療群 2～4）米国人及び非米国人被験者の大部分が、以前の治療よりコンシズマブによる予防治療を好むと回答した。

36-Item Short Form Health Survey（SF-36v2）－米国人対非米国人

コンシズマブによる予防治療を受けた被験者（治療群 2～4）のベースラインの平均値は、全体的に非米国人被験者と比較して 5 例の米国人被験者において高かった（付録 2.7.3.7.1、Table 21～Table 30）。

コンシズマブによる予防治療を受けた米国人被験者 5 例及び非米国人被験者（治療群 2～4）はともに、すべての各健康尺度（米国人被験者において「社会生活機能」のスコアは減少したことを除く）ならびに「身体的側面の QOL サマリースコア」及び「精神的側面の QOL サマリースコア」の平均値はベースラインから 24 週で改善が認められ、これはいずれのグループにおいても機能的健康及びウェルビーイングが改善したことを示していた（表 2.7.3.3-21）。SF-36v2 の米国人及び非米国人被験者の週別の各健康尺度は付録 2.7.3.7.1、Table 21～Table 30 に示す。

表 2.7.3.3-21　SF-36v2（標準版）－米国人対非米国人－記述統計量－HAwI+HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Change from baseline to week 24 - Bodily pain		
N	3	63
Median	6.5	4.8
P25 ; P75	-3.6 ; 15.7	0.0 ; 12.5
Mean (SD)	6.2 (9.7)	7.0 (9.8)
Min ; Max	-3.6 ; 15.7	-13.3 ; 29.8
Change from baseline to week 24 - Physical functioning		
N	3	63
Median	3.8	3.8
P25 ; P75	1.9 ; 5.8	0.0 ; 7.7
Mean (SD)	3.8 (1.9)	4.1 (7.1)
Min ; Max	1.9 ; 5.8	-15.3 ; 30.6
Change from baseline to week 24 - Role - Physical		
N	3	63
Median	4.5	4.5
P25 ; P75	0.0 ; 4.5	0.0 ; 13.5
Mean (SD)	3.0 (2.6)	5.6 (9.6)
Min ; Max	0.0 ; 4.5	-18.0 ; 26.9
Change from baseline to week 24 - General Health		
N	3	63
Median	0.0	4.8
P25 ; P75	-2.4 ; 6.2	0.0 ; 12.8
Mean (SD)	1.3 (4.4)	6.0 (10.5)
Min ; Max	-2.4 ; 6.2	-13.3 ; 34.2
Change from baseline to week 24 - Vitality		
N	3	63
Median	8.9	5.9
P25 ; P75	-5.9 ; 14.9	0.0 ; 11.9
Mean (SD)	5.9 (10.7)	6.5 (10.3)
Min ; Max	-5.9 ; 14.9	-26.7 ; 41.6
Change from baseline to week 24 - Social Functioning		
N	3	63
Median	0.0	5.0
P25 ; P75	-10.0 ; 0.0	0.0 ; 10.0
Mean (SD)	-3.3 (5.8)	6.4 (10.8)
Min ; Max	-10.0 ; 0.0	-15.0 ; 40.1
Change from baseline to week 24 - Role - Emotional		
N	3	63
Median	3.5	0.0
P25 ; P75	0.0 ; 7.0	0.0 ; 10.4
Mean (SD)	3.5 (3.5)	4.2 (10.0)
Min ; Max	0.0 ; 7.0	-31.3 ; 31.3

Continues on next page

SF-36 v2 (standard version) - bodily pain - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311 - Continued

	Concizumab PPX (arms 2-4)	
	US	non-US
Change from baseline to week 24 - Mental Health		
N	3	63
Median	2.6	2.6
P25 ; P75	-2.6 ; 2.6	-2.6 ; 10.5
Mean (SD)	0.9 (3.0)	4.3 (11.6)
Min ; Max	-2.6 ; 2.6	-15.7 ; 36.6
Change from baseline to week 24 - Physical health component score		
N	3	63
Median	5.1	6.1
P25 ; P75	-0.3 ; 8.2	0.7 ; 11.0
Mean (SD)	4.3 (4.3)	5.8 (7.7)
Min ; Max	-0.3 ; 8.2	-9.6 ; 28.6
Change from baseline to week 24 - Mental health component score		
N	3	63
Median	3.2	3.2
P25 ; P75	-5.8 ; 4.3	-2.4 ; 10.1
Mean (SD)	0.6 (5.5)	4.8 (10.9)
Min ; Max	-5.8 ; 4.3	-12.5 ; 37.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Notes: Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a－米国人対非米国人

全集団においてすべての治療群でみられた PROMIS Numeric Rating Scale v. 1.0 Pain Intensity 1a により評価された痛みの強度の低下〔4311 試験（Module 5.3.5.1）Section 11.6.2〕は、米国人被験者 5 例及び非米国人被験者でも認められた（付録 2.7.3.7.1、Table 31）。

コンシズマブによる予防治療を受けた米国人被験者 5 例及び非米国人被験者（治療群 2～4）のベースラインスコアの平均値は同程度であった（付録 2.7.3.7.1、Table 31）。ベースラインから 24 週でスコアの平均値は米国人被験者 5 例及び非米国人被験者ともに低下し、いずれのグループでも痛みの強度が低下したことを示していた。変化量の平均値は、米国人被験者で-1.3、非米国人被験者で-1.1 であった。

PROMIS Short Form v. 2.0 Upper Extremity 7a－米国人対非米国人

PROMIS Short Form v2.0 Upper Extremity 7a により評価された米国人及び非米国人被験者の身体機能の結果を付録 2.7.3.7.1、Table 32 に示す。

ベースラインスコアの平均値は、コンシズマブによる予防治療を受けた（治療群 2～4）米国人被験者 5 例では 47.5、非米国人被験者では 39.8 であった（付録 2.7.3.7.1、Table 32）。ベースラインから 24 週でスコアの平均値は米国人被験者 5 例では 0.2 ポイント減少し、身体機能がわずかに低下したことを示していた。非米国人被験者では 3.4 ポイント増加し、身体機能が改善したことを示していた。

成人血友病患者用 QOL 質問票（Haem-A-QoL）－米国人対非米国人

Haem-A-QoL により評価された米国人及び非米国人被験者の生活の質の結果を付録 2.7.3.7.1、Table 33～Table 43 に示す。24 週のデータに貢献したコンシズマブによる予防治療を受けた（治療群 2～4）米国人被験者はいなかったため、米国人及び非米国人被験者間の Haem-A-QoL スコアのベースラインから 24 週までの変化量の比較はできなかった。

身体機能に関する重症度に対する患者の全般的印象（PGI-S）－米国人対非米国人

コンシズマブによる予防治療を受けた米国人及び非米国人被験者（治療群 2～4）の週別の PGI-S の結果の要約を付録 2.7.3.7.1、Table 51 に示す。

ベースライン時に質問票に回答した米国人被験者 3 例では、ベースラインの身体機能のレベルの回答は「良い」（66.7%）、「悪い」（33.3%）であり、ベースライン時に質問票に回答した非米国人被験者 59 例では、ベースラインの身体機能のレベルの回答は「非常に良い」（8.5%）、「良い」（32.2%）、「まずまず」（33.9%）、「悪い」（10.2%）、「非常に悪い」（15.3%）であった。

24 週（来院 9／9a）に質問票に回答した米国人被験者 5 例において、24 週（来院 9／9a）の身体機能のレベルの回答は「非常に良い」（20.0%）、「良い」（60.0%）、「まずまず」（20.0%）であり、24 週（来院 9／9a）に質問票に回答した非米国人被験者 78 例において、24 週（来院 9／9a）の身体機能のレベルの回答は「非常に良い」（26.9%）、「良い」（39.7%）、「まずまず」（26.9%）、「悪い」（6.4%）であった。

身体機能に関する変化に対する患者の全般的印象（PGI-C）－米国人対非米国人

コンシズマブによる予防治療を受けた米国人及び非米国人被験者（治療群 2～4）の大部分がコンシズマブによる治療を開始後、身体機能が改善したと報告した（付録 2.7.3.7.1、Table 52）。

24 週（来院 9／9a）において、コンシズマブによる治療を開始後、質問票に回答した米国人被験者 5 例が身体機能に関して「非常に良くなった」（60.0%）又は「まあまあ良くなった」（20.0%）と回答し、20.0%が「変化なし」と回答した。24 週（来院 9／9a）において、質問票に回答した非米国人被験者 78 例が身体機能に関して「非常に良くなった」（55.1%）、「まあまあ良くなった」（29.5%）又は「少し良くなった」（10.3%）と回答し、5.1%が「変化なし」と回答した（付録 2.7.3.7.1、Table 52）。

Haemophilia Patient Preference Questionnaire（H-PPQ）－米国人対非米国人

コンシズマブによる予防治療を受けた米国人及び非米国人被験者（治療群 2～4）の大部分が以前の治療よりコンシズマブによる予防治療を好むと回答した（付録 2.7.3.7.1、Table 50）。

コンシズマブによる予防治療を受け、質問票に回答した米国人被験者（治療群 2～4）5 例のうち、4 例（80%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、1 例が特に好みはないと回答した。

コンシズマブによる予防治療を受け、質問票に回答した非米国人被験者（治療群 2～4）78 例のうち、73 例（93.6%）が以前の治療よりコンシズマブによる予防治療を好むと回答し、4 例が特に好みはないと回答し、1 例がコンシズマブによる予防治療より以前の治療を好むと回答した。16 例は回答しなかった（付録 2.7.3.7.1、Table 50）。

血友病治療経験評価（Hemo-TEM）－米国人対非米国人

コンシズマブによる予防治療を受けた被験者（治療群 2～4）では、ベースラインにおける Hemo-TEM スコアは非米国人被験者と比較して米国人被験者 5 例において低く、米国人被験者においてベースラインの治療の負担が少なかったことを示していた。

コンシズマブによる予防治療を受けた米国人被験者 5 例及び非米国人被験者（治療群 2～4）いずれにおいても、ベースラインから 24 週までの Hemo-TEM 総スコア及び各ドメインスコアの低下が認められ、治療の負担の軽減が示された（表 2.7.3.3-22）。

ベースラインから 24 週までの Hemo-TEM 総スコアは平均して、米国人被験者では 12.4 ポイント、非米国人被験者では 17.0 ポイント改善した（付録 2.7.3.7.1、Table 44）。

米国人被験者及び非米国人被験者の週別の Hemo-TEM の各ドメインの結果を付録 2.7.3.7.1、Table 44～Table 49 に示す。

表 2.7.3.3-22　Hemo-TEM－ベースラインから 24 週までの変化量－米国人対非米国人－記述統計量－HAwI+HBwI－OTexIR－最大の解析対象集団－4311 試験

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Change from baseline to week 24 - Total score		
N	3	58
Median	-11.7	-9.8
P25 ; P75	-20.3 ; -5.2	-27.7 ; 0.0
Mean (SD)	-12.4 (7.6)	-17.0 (22.7)
Min ; Max	-20.3 ; -5.2	-81.3 ; 13.2
Change from baseline to week 24 - Injection difficulties		
N	3	58
Median	-16.7	-8.3
P25 ; P75	-41.7 ; 8.3	-33.3 ; 0.0
Mean (SD)	-16.7 (25.0)	-17.5 (30.7)
Min ; Max	-41.7 ; 8.3	-100 ; 50.0
Change from baseline to week 24 - Physical impact		
N	3	58
Median	-20.8	-6.3
P25 ; P75	-33.3 ; -4.2	-20.8 ; 0.0
Mean (SD)	-19.4 (14.6)	-13.9 (21.3)
Min ; Max	-33.3 ; -4.2	-66.7 ; 12.5
Change from baseline to week 24 - Interference		
N	3	58
Median	0.0	-17.7
P25 ; P75	-18.8 ; 6.3	-41.7 ; 0.0
Mean (SD)	-4.2 (13.0)	-24.4 (31.6)
Min ; Max	-18.8 ; 6.3	-100 ; 18.8
Change from baseline to week 24 - Treatment bother		
N	3	58
Median	-7.1	-8.9
P25 ; P75	-28.6 ; 0.0	-28.6 ; 0.0
Mean (SD)	-11.9 (14.9)	-15.8 (29.2)
Min ; Max	-28.6 ; 0.0	-92.9 ; 85.7
Change from baseline to week 24 - Emotional impact		
N	3	58
Median	-12.5	-4.2
P25 ; P75	-16.7 ; 0.0	-20.8 ; 0.0
Mean (SD)	-9.7 (8.7)	-13.4 (25.2)
Min ; Max	-16.7 ; 0.0	-100 ; 25.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

2.7.3.4　推奨用法・用量に関する臨床情報の解析

コンシズマブは標的介在性の薬物動態（TMDD）の影響を受け、曝露量について大きな被験者間及び被験者内変動を伴う（Module 2.7.2.3.1.2.3）。これは TMDD が標的介在性のクリアランスに影響を与えるためである。すなわち、コンシズマブの血漿中濃度が低いときクリアランスは高くなり（消失は早くなり）、コンシズマブの血漿中濃度が高いときクリアランスは低くなる（消失は遅くなる）。コンシズマブの投与方法においては、コンシズマブの血漿中曝露量に基づき維持用量を設定することでこの変動を考慮した。

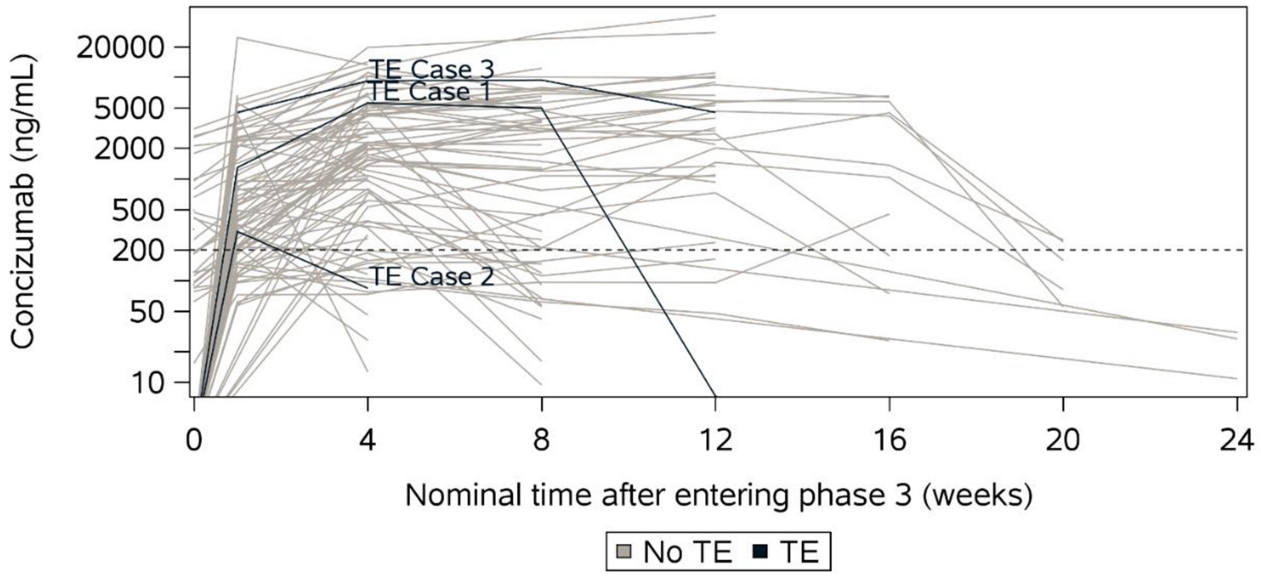
コンシズマブの推奨用法・用量（コンシズマブによる治療の一時中断後に導入された）を図 2.7.3.1-4 に示した。当該投与方法では、初回投与時に負荷投与としてコンシズマブ 1.0 mg/kg を投与し、2 日目以降は個々の維持用量を設定するまでコンシズマブ 0.20 mg/kg を 1 日 1 回投与した。投与開始から 4 週後にコンシズマブの血漿中濃度を測定し、コンシズマブの曝露量に基づき維持用量を以下の通り設定する。

- 200 ng/mL 未満：1 日 1 回 0.25 mg/kg
- 200～4000 ng/mL：1 日 1 回 0.20 mg/kg
- 4000 ng/mL 超：1 日 1 回 0.15 mg/kg

コンシズマブの投与方法は第 2 相試験及び第 3 相試験開始初期のデータの詳細な分析に基づき設定された。

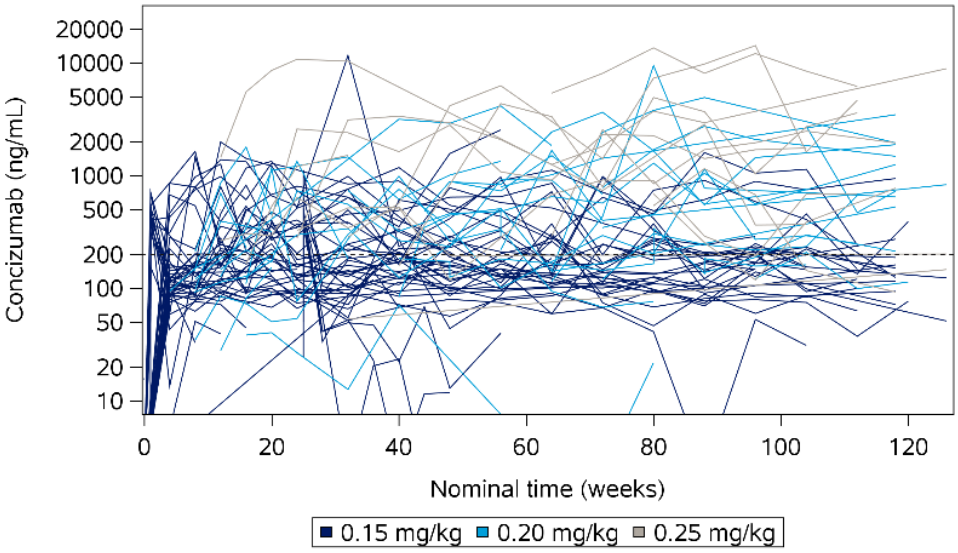
初期の 1 日用量である 0.20 mg/kg（第 3 相試験の再開後に 0.25 mg/kg から減量：詳細は 2.7.3.1.2.1 に提示）は、集団レベルでのコンシズマブ曝露量を低下させるために導入された。重篤な血栓塞栓性事象を発現した被験者のうち 2 例において、コンシズマブの曝露量（コンシズマブの治療再開前）が第 2 相及び第 3 相試験で認められた曝露量範囲の中でより高い範囲に含まれていたこと（図 2.7.3.4-1 及び図 2.7.3.4-2）、ならびに全般的に第 3 相試験で観察されたコンシズマブの曝露量が予想よりも高かったことに基づいて、開始用量の減量が行われた。

図 2.7.3.4-1　　コンシズマブ 1 mg/kg を負荷投与し、その後維持用量として 1 日 1 回、0.25 mg/kg を投与したときの曝露量（観測値）－血栓塞栓性事象を発現した被験者と発現していない被験者（第 3 相試験：4311 試験及び 4307 試験）



Abbreviations: TE = thromboembolic event. **Notes**: The cut-off date for these results is April 27, 2020. The horizontal dashed line indicated the target concizumab exposure level above 200 ng/mL.

図 2.7.3.4-2　　第 2 相試験（4310 試験及び 4255 試験）における曝露量（観測値）



Notes: the observed exposure in the phase 2 trials is shown by dose level. The horizontal dashed line indicated the target concizumab exposure level above 200 ng/mL.

維持用量の設定の実施は、主に減量された初期の 1 日用量（0.20 mg/kg）により一部の被験者で出血回数が増加しないようにするために導入された。

コンシズマブの維持用量のための cut-off の下限である 200 ng/mL は、第 2 相試験（4255 試験及び 4310 試験）の主要パートの結果に基づいて実施した探索的な曝露量-反応解析から得られたものである。薬物動態モデル及び曝露量-反応解析の詳細については、「NN7415-4255 and NN7415 4310 Population PK and exposure-response analysis report」（Module 5.3.3.5）に示す。この薬物動態モデルは、第 2 相試験におけるコンシズマブの薬物動態を適切に示しており、出血時の個々のコンシズマブ濃度

を推定することが可能であった。各被験者からのコンシズマブの曝露量を曝露量間隔ごとに分け、各間隔に対して様々なパラメータを要約した（表 2.7.3.4-1 参照）。高用量のバイアスを避けるため、被験者が 0.15 mg/kg を投与されていた期間のみを含めた。これは、高用量の投与を受けた被験者は、事前の定義から出血が多い被験者と考えられたためである。このように、表 2.7.3.4-1 に示した曝露量-反応解析から、コンシズマブ 200 ng/mL までの曝露量では、全体の出血率は比較的高いことが示された。一方、200 ng/mL を超えると、出血率が低くなる傾向がある。なお、特定の曝露量間隔（特に 500 ng/mL を超えた曝露量）における出血回数と曝露期間のデータは限られていることに注意が必要である。これに基づき、ノボ ノルディスク社はコンシズマブの維持用量のための cut-off の下限として 200 ng/mL を選択した。この下限値は、4311 試験の結果からも支持されている〔Modelling report（Module 5.3.3.5）、Figure 1-3 及び Figure 1-4〕。

表 2.7.3.4-1　　モデルより算出した年換算の出血率の曝露量－反応解析

Exposure level (ng/mL)	Number of patients	Proportion with bleeding episodes (%)	Number of bleeding episodes	Exposure time (years)	ABR estimate (bleeds/year)	ABR 95% CI
0-100	53	55	65	6.72	15.6	10.1-24.1
100-200	48	62	92	8.88	14.5	8.1-26.2
200-500	26	46	22	5.06	4.9	2.2-10.7
500-1000	13	38	8	2.35	3.7	1.2-10.8
>1000	8	38	5	0.98	5.4	1.4-19.2

ABR: Annual bleeding rate estimated from the binomial model. CI: Confidence interval.

初期の 1 日用量を 0.20 mg/kg に減量したことに加えて、追加の注意事項として、被験者におけるコンシズマブの曝露量が非常に高い〔すなわち無毒性量（NOAEL：82,600 ng/mL）に近い（Module 2.6.6、表 2.6.6-17）〕レベルで維持されることを避けるために、極めて慎重なアプローチとして曝露量の上限を 4000 ng/mL と設定した。コンシズマブへの高い曝露自体が血栓塞栓性事象の原因であることを示すデータがないものの、重篤な血栓塞栓性事象を発現した被験者のうち 2 例の再開前の曝露量が第 2 相及び第 3 相試験で観察された曝露量範囲のうち比較的高い範囲に含まれていたことは、血栓塞栓性事象のリスクが高いこと及び破綻出血治療での高用量又は頻回投与と合わせて、血栓塞栓性事象発現の 1 つの要因になりうることを示唆している。3813 試験（健康被験者及び血友病患者を対象とした第 1 相試験：Module 2.7.2、表 2.7.2.2-1）では、非常に高いコンシズマブ血漿中濃度（100,000 ng/mL 超）に約 48 時間曝露された被験者がいた。本被験者の C_{max} は 239,053 ng/mL であったが、安全性に問題は認められなかった（Module 2.7.2、図 2.7.2.3-1 及び表 2.7.2.3-1）。

第 3 相試験（4311 試験）の治療再開後に用いられた投与方法におけるヒトでの曝露量（C_{max}）の幾何平均値（1167 ng/mL：Module 2.7.2、表 2.7.2.3-4）は、NOAEL よりも低かった（NOAEL はヒトでの曝露量の 70 倍以上高かった）。

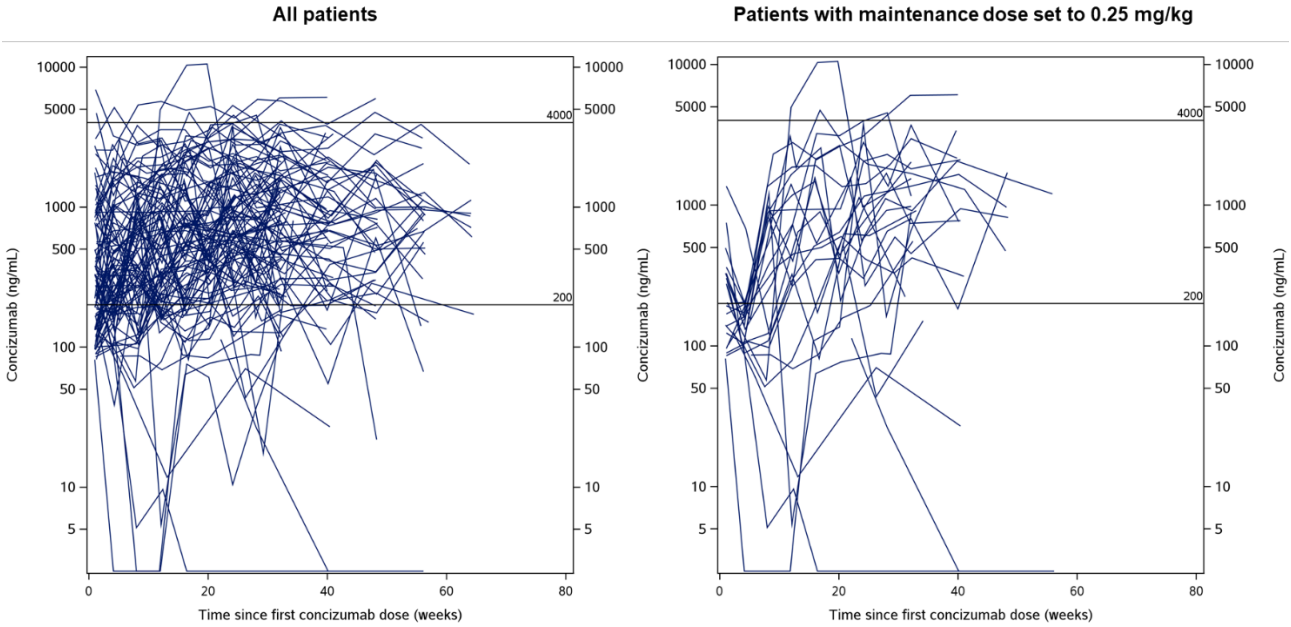
4311 試験における個々の被験者の投与前のコンシズマブ血漿中濃度（C_{trough}）を図 2.7.3.4-3 に示す。

4311 試験において、コンシズマブの曝露量の範囲は被験者ごとに維持用量を設定した後安定した（図 2.7.3.4-3、左図）。OTexIR 解析データセットにおいて、コンシズマブの投与を受けた被験者（治

療群 2、3 及び 4）は 99 例であった。2 例の被験者が来院 4 前に投与を中止したため、維持用量が報告されなかった。残りの 97 例のうち 72 例（74.2%）が 0.20 mg/kg の用量を維持し、24 例（24.7%）が 0.25 mg/kg に増量し、1 例（1.0%）が 0.15 mg/kg に減量した〔4311 試験（Module 5.3.5.1）TFL Table 14.2.10〕。図 2.7.3.4-3 の右図に示すとおり、用量を 0.25 mg/kg に増量した被験者の曝露量は増加した。

各部分集団における曝露量については Module 2.7.2.3.1.4 に示す。

図 2.7.3.4-3　コンシズマブの血漿中濃度推移－試験再開後の投与方法－HAwI+HBwI－OTexIR－安全性解析対象集団



Notes: Each line represents a patient on concizumab PPX (arms 2, 3 and 4). Horizontal lines at 200 and 4000 ng/mL represent exposure thresholds used for maintenance dose setting. Note that some patients had temporary treatment discontinuations and some patients had their individual maintenance dose set later than the per protocol expiry of the dose adjustment period (5−8 weeks after treatment initiation).

治療再開後 4311 試験において改訂された投与方法に基づくコンシズマブによる予防治療（図 2.7.3.1-4）は、インヒビターを有する血友病 A 及び B 患者において、出血時治療と比較して、すべての出血に関するエンドポイント及び観察項目を通じて年換算の出血率の低下に対して効果があることが示された（2.7.3.3.2.1.1 項）。

出血エピソードに関する曝露量－反応解析から、このコンシズマブの投与方法により効果が横ばい（プラトー）となる濃度が維持されることが示された〔Modelling report（Module 5.3.3.5）Section 7.2〕。シミュレーションから、被験者ごとの維持用量の設定によりコンシズマブの曝露量の全体的な集団レベルばらつきは小さくなることが支持された〔Modelling report（Module 5.3.3.5）Section 8.1〕。

上記の結果ならびに安全性及び忍容性の結果から、図 2.7.3.1-4 に示すコンシズマブの投与方法はインヒビターを保有する成人及び青年の血友病 A 及び B 患者に対する予防治療に推奨される。

2.7.3.5 効果の持続、耐薬性

効果の持続

コンシズマブの効果の持続は第 2 相試験の 4255 試験及び 4310 試験の主要及び延長パートを通じた有効性の結果の一貫性から示されている。

4255 試験において、主要及び延長パート後（76 週間以上後）の有効性、薬物動態及び薬力学的作用パラメータの結果は主要パート後（24 週間以上後）の結果と一貫していた。同様に 4310 試験においても、主要及び延長パート後（76 週間以上後）の有効性、薬物動態及び薬力学的作用パラメータの結果は主要パート後（24 週間以上後）の結果と一貫していた。

詳細は各試験の治験総括報告書〔4255 試験 主要パート（Module 5.3.5.2）、4255 試験 延長パート（Module 5.3.5.2）、4310 試験 主要パート（Module 5.3.5.1）及び 4310 試験 延長パート（Module 5.3.5.1）〕に示す。

第 2 相試験の 4310 試験に組み入れられたインヒビターを保有する血友病 A 及び B 患者は、4311 試験の治療群 3 へ移行することを提案された。これらの被験者は 4311 試験へ組み入れられるまでコンシズマブによる予防治療を継続することを求められた。4311 試験では来院 1 及び 2 を合わせて実施し、すべての被験者が 0.25 mg/kg の用量で投与を開始した〔4311 試験（Module 5.3.5.1）Section 9.1〕。このことから、コンシズマブの効果の持続は、4310 試験と 4311 試験の両方でコンシズマブの投与を受けた 4311 試験のコンシズマブによる予防治療群（治療群 3）の被験者から得られた有効性の結果によりさらに支持された。

4311 試験のコンシズマブによる予防治療群（治療群 3）の被験者は 4310 試験及び 4311 試験において異なる投与方法でコンシズマブの投与を受けたことに留意する必要があるものの、4310 試験の終了後に 4311 試験においてコンシズマブによる治療を継続すること及び治療の一時中断後も 4311 試験で投与を継続することを選択した。

第 2 相試験（4310 試験）で組み入れられ 4311 試験の治療群 3 に割り当てられた被験者の曝露期間の平均値は、4311 試験（OTwoATexIR 解析データセットに基づく）において 44.4 週間〔4311 試験（Module 5.3.5.1）TFL Tables 14.2.19〕であり、さらに少なくとも 4310 試験の延長パート（52～94 週間）においても曝露を受けた（図 2.7.3.1-2）。

耐薬性－抗体発現

インヒビターの発生（血友病 A 患者においては抗 FVIII 抗体、血友病 B 患者においては抗 FIX 抗体であり、いずれも *in vivo* において中和作用を有する）は、血友病治療において最も深刻で困難な合併症である。コンシズマブに対する抗体の発生はコンシズマブの曝露量を変化させ、コンシズマブの有効性を間接的に変化させる可能性がある。また、抗コンシズマブ抗体はコンシズマブの TFPI への結合を阻害する（薬物に対する中和作用）ことにより直接有効性に影響を与える可能性もある。

抗薬物抗体（コンシズマブに結合する抗体）及び *in vitro* 中和作用を有する抗薬物抗体は臨床試験全体を通じて監視された。

第 2 相試験（4310 試験及び 4255 試験）期間中に、コンシズマブの投与を受けた 61 例中 15 例（24～25%）において、最初の投与以降に抗薬物抗体が陽性となった。抗薬物抗体が陽性となった被験者は 1 例を除き、力価は低く（低レベル）、範囲は 1～32（最小希釈倍率の 100 倍を掛けた場合は 100～

3200）であった。抗薬物抗体が陽性となった被験者のうち 4 例（6.6%）でコンシズマブに対する *in vitro* 中和作用が認められた。抗薬物抗体が陽性となった被験者において、出血パターン、有害事象、薬物動態、又は薬力学的作用データに対する抗薬物抗体の明らかな影響は認められなかった。

4310 試験の 1 例において、抗薬物抗体の力価が最初は低かったが数ヵ月の後上昇し高くなった（低レベルから高レベルにシフト）。これは手術によるコンシズマブ投与の一時的な中止後のコンシズマブの投与再開と同時に起きた外傷による免疫システムの亢進によって起こった可能性がある。当該被験者は、*in vitro* 中和作用を有する抗薬物抗体が認められ、遊離 TFPI 濃度がベースライン値に戻ったが、抗薬物抗体の臨床的影響について結論は得られていない〔Integrated summary of immunogenicity（Module 5.3.5.3）Section 4.8〕。

4311 試験においては、抗薬物抗体の評価はコンシズマブの投与を受けたすべての被験者に対して行った。治療の一時中断前及び後にコンシズマブによる予防治療を受けた（治療群 1～4）127 例のうち、33 例（26%）がコンシズマブの投与を最初に受けた後に 1 回以上抗コンシズマブ抗体が陽性になった。127 例のうち 21 例が第 2 相試験の 4310 試験でもコンシズマブの投与を受けていた。このうち 2 つの試験で抗コンシズマブ抗体が陽性になったのは 1 例のみであった〔Integrated summary of immunogenicity（Module 5.3.5.3）Section 4.3.3〕。

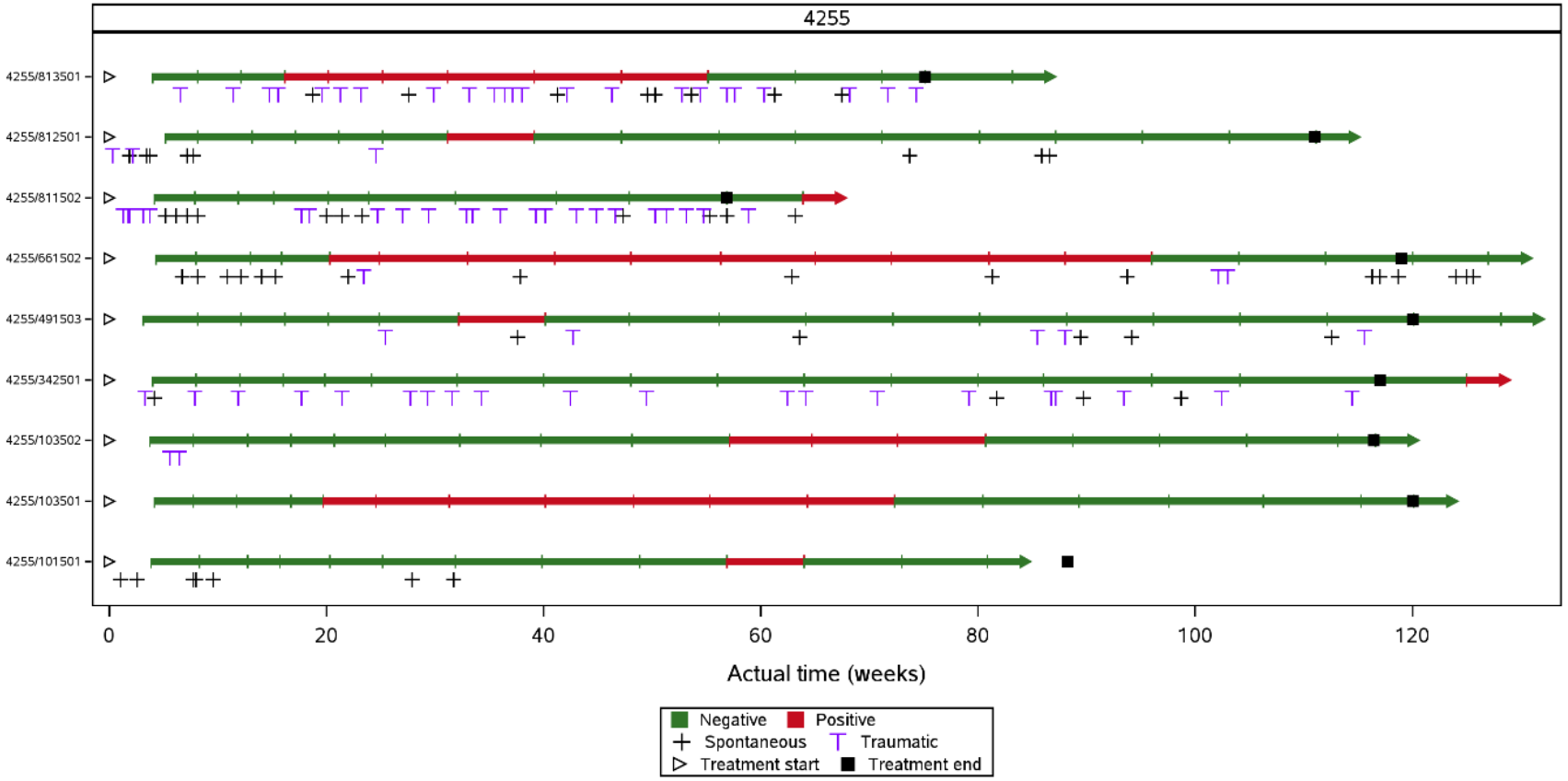
一時的に力価が中レベルである 25600〔最小希釈倍率（抗薬物抗体の力価アッセイの希釈ステップにおける希釈率）の 100 倍を掛けた値〕に到達した 1 例を除き、力価の範囲は 100～6400〔最小希釈倍率の 100 倍を掛けた値〕であった〔抗体価の基準については Integrated summary of immunogenicity（Module 5.3.5.3）Section 3.4.1.4 に提示する〕。コンシズマブに結合する抗薬物抗体の感度は 1 ng/mL 未満であり、これらは非常に低い力価と考えられた。抗薬物抗体陽性の 8 例（6.3%）は試験中 1 回以上 *in vitro* 中和抗体が陽性となった。抗薬物抗体が陽性となった被験者及び *in vitro* 中和作用を有する抗薬物抗体が陽性となった被験者において、出血パターン、有害事象、薬物動態、又は薬力学的作用データに対する抗薬物抗体の明らかな影響は認められなかった〔Integrated summary of immunogenicity（Module 5.3.5.3）Section 5.1〕。

患者ごとのコンパッショネートユースでコンシズマブの投与を受けた 1 例（2 年 3 ヵ月間）では、効果が減弱した（消失はしていない）期間において、*in vitro* 中和作用を有する抗コンシズマブ抗体が 1 回陽性となった〔Integrated summary of immunogenicity（Module 5.3.5.3）Section 4.9.2〕。効果の減弱がみられた以降、有害事象は報告されておらず、患者はコンシズマブによる治療を継続した〔コンパッショネートユース報告書（Module 5.3.5.4）Section 5.1.6〕。さらに、コンパッショネートユースプログラムの患者 1 例では、来院 2 及び 3 において抗コンシズマブ抗体が陽性であった。抗薬物抗体の力価は低く（低レベル）〔Integrated summary of immunogenicity（Module 5.3.5.3）Section 4.9.1〕、当該患者において有害事象は報告されなかった〔コンパッショネートユース報告書（Module 5.3.5.4）Section 5.2.1〕。

抗コンシズマブ抗体がコンシズマブの有効性に及ぼす影響は、投与期間中に 1 時点以上で抗コンシズマブ抗体が陽性であった被験者について、治療された自然出血及び外傷性出血エピソードの経時的な発現パターンを抗薬物抗体の状態（有無）とあわせて評価することによって検討した。結果を図 2.7.3.5-1、図 2.7.3.5-2、図 2.7.3.5-3 に示す。

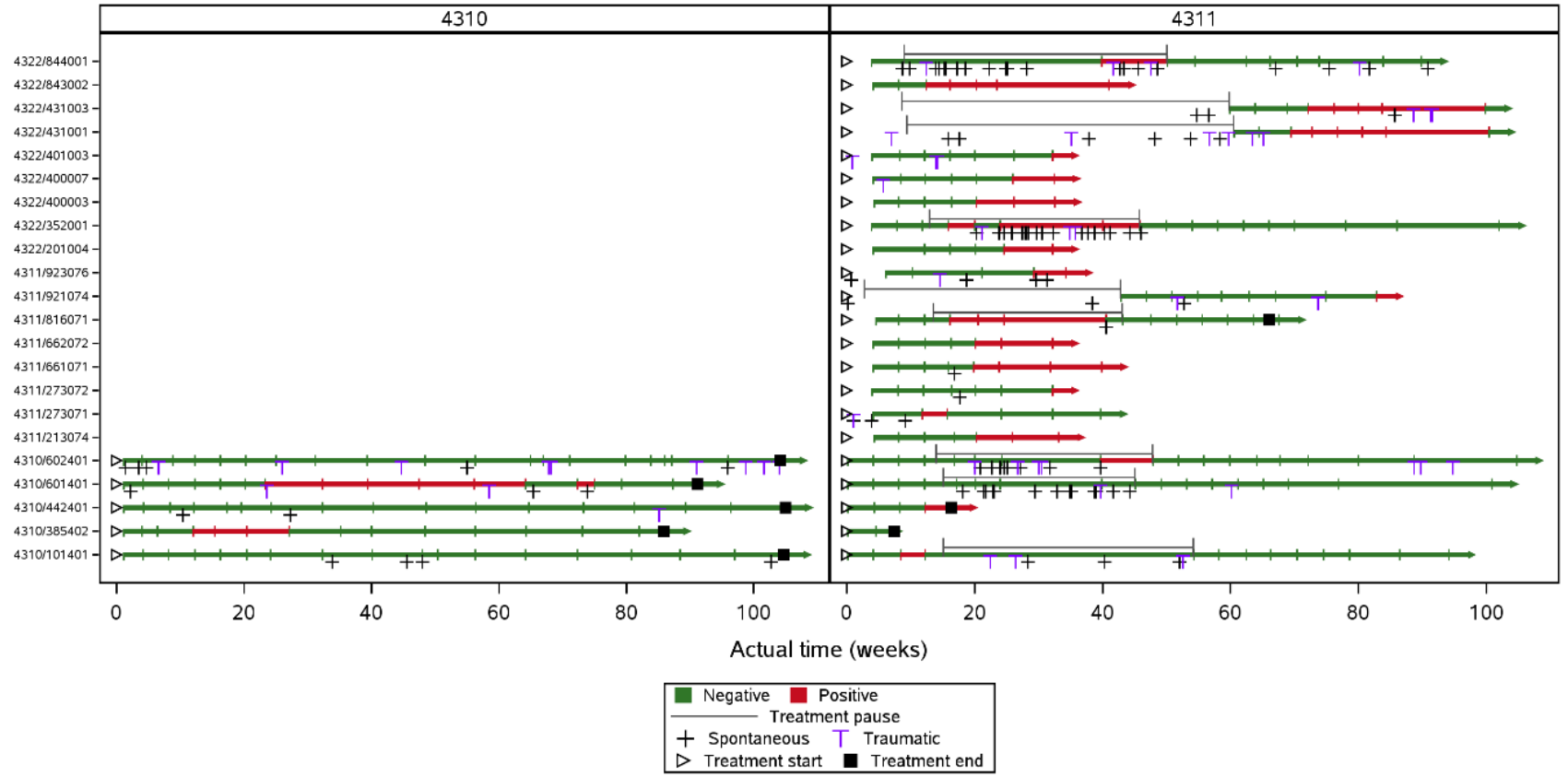
各被験者の治療された自然出血及び外傷性出血エピソードの発現パターンは、抗コンシズマブ抗体の有無（発生期間及び非発生期間）で概ね異なることはなかった。これらの結果から、抗コンシズマブ抗体の発生は、血友病患者におけるコンシズマブの出血予防効果に影響を及ぼさないと考えられた。

図 2.7.3.5-1　出血エピソードの経時的な発現状況と抗薬物抗体の状態－ 抗薬物抗体陽性被験者－インヒビターを保有しない血友病 A 患者－安全性解析対象集団



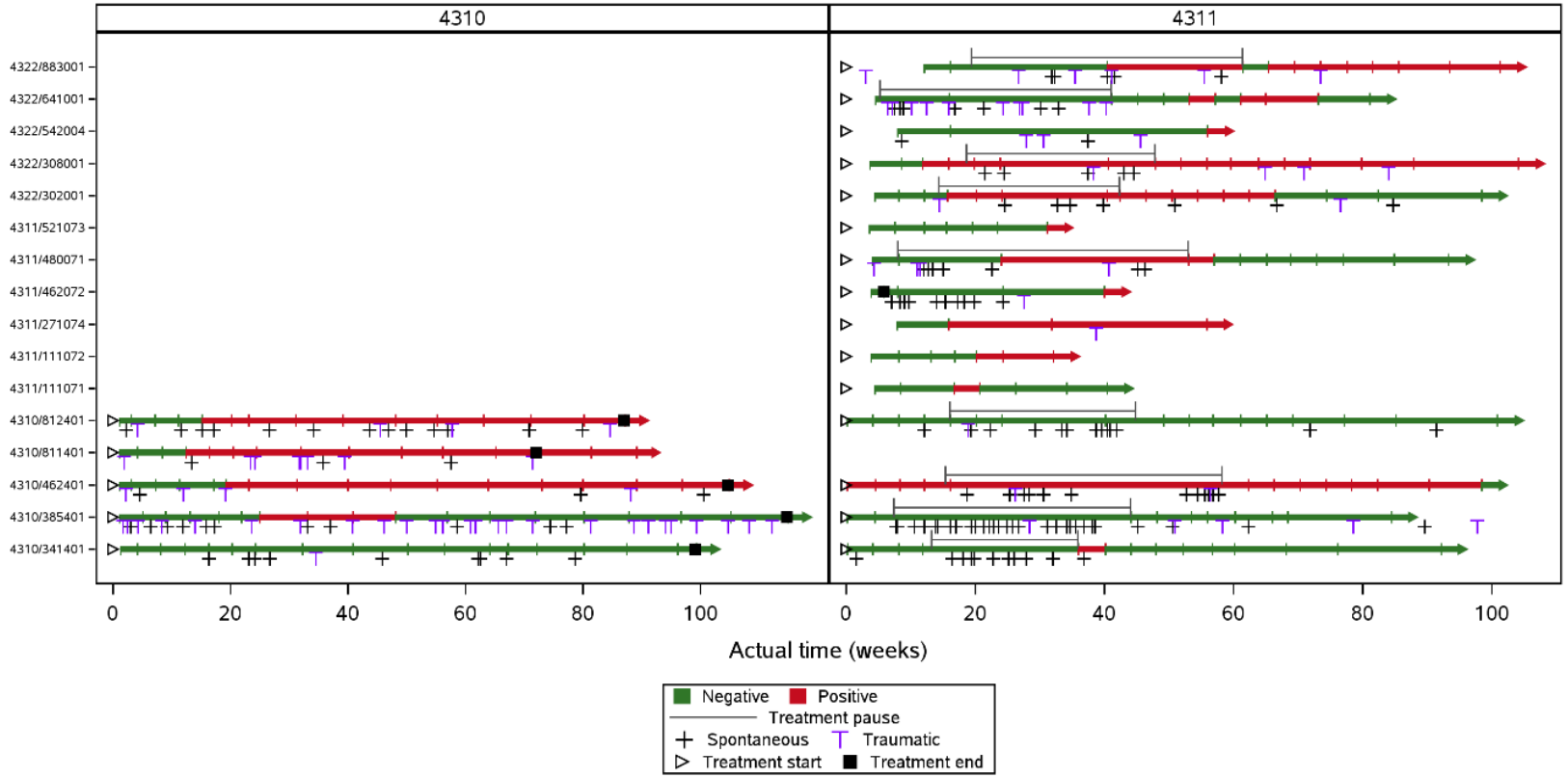
ADA: Anti-concizumab antibody; HA: haemophilia A without inhibitors
The plot includes all patients who were positive for ADAs at one or more timepoints after first concizumab dose. Patients were exposed to concizumab from treatment start to treatment end.
Only treated bleeding episodes are marked under the ADA status line of each subject

図 2.7.3.5-2　出血エピソードの経時的な発現状況と抗薬物抗体の状態－抗薬物抗体陽性被験者－インヒビターを保有する血友病 A 患者－安全性解析対象集団



ADA: Anti-concizumab antibody; HAwI: haemophilia A with inhibitors
The plot includes all patients who were positive for ADAs at one or more timepoints after first concizumab dose. Patients were exposed to concizumab from treatment start to treatment end except during the treatment pause for patients receiving first concizumab dose in trial before the pause.
Only treated bleeding episodes are marked under the ADA status line of each subject

図 2.7.3.5-3　　出血エピソードの経時的な発現状況と抗薬物抗体の状態－抗薬物抗体陽性被験者－インヒビターを保有する血友病 B 患者－安全性解析対象集団



ADA: Anti-concizumab antibody; HBwI: haemophilia B with inhibitors
The plot includes all patients who were positive for ADAs at one or more timepoints after first concizumab dose. Patients were exposed to concizumab from treatment start to treatment end except during the treatment pause for patients receiving first concizumab dose in trial before the pause.
Only treated bleeding episodes are marked under the ADA status line of each subject

コンシズマブの開発プログラムを通じたコンシズマブの免疫原性評価の結果に関する詳細はIntegrated summary of immunogenicity（Module 5.3.5.3）Section 4 に示す。

全体として、これらの結果はコンシズマブの忍容性を支持するものであった。

2.7.3.6 参考文献

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コンシズマブ（遺伝子組換え）

2.7.3.7. 付録
1. 表、図及び一覧

ノボ ノルディスク ファーマ株式会社

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7.1 Summary of Clinical Efficacy

1 Demograhics and baseline characteristics - Japanese subjects - summary - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX			Total
	(arm 1) N (%)	(arm 2) N (%)	(arm 3) N (%)	(arm 4) N (%)	N (%)
Number of subjects	1	1	1	3	6
Age group (years)					
Adolescents (12-17 years)	0	0	0	1 (33.3)	1 (16.7)
Adults (18-64 years)	1 (100)	1 (100)	1 (100)	2 (66.7)	5 (83.3)
Elderly/very elderly (65-84 years)	0	0	0	0	0
Ethnicity					
Hispanic or Latino	0	0	0	0	0
Not Hispanic or Latino	1 (100)	1 (100)	1 (100)	3 (100)	6 (100)
Not Reported	0	0	0	0	0
Race					
American Indian or Alaska Native	0	0	0	0	0
Asian	1 (100)	1 (100)	1 (100)	3 (100)	6 (100)
Black or African American	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
White	0	0	0	0	0
Not Reported	0	0	0	0	0
Country					
Japan	1 (100)	1 (100)	1 (100)	3 (100)	6 (100)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen.
N: number of subjects, %: percentage of subjects. Baseline is defined as the latest measurement before first dose with new regimen or before randomisation for arm 1.
Note: information on age, ethnicity and race are according to local regulations.

2 Demograhics and baseline characteristics - Japanese subjects - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX			Total
	Arm 1	Arm 2	Arm 3	Arm 4	
Number of subjects	1	1	1	3	6
Age(years)					
N	1	1	1	3	6
Median	39.0	30.0	47.0	33.0	36.0
P25 ; P75	39.0 ; 39.0	30.0 ; 30.0	47.0 ; 47.0	15.0 ; 41.0	30.0 ; 41.0
Mean (SD)	39.0 (.)	30.0 (.)	47.0 (.)	29.7 (13.3)	34.2 (11.1)
Min ; Max	39.0 ; 39.0	30.0 ; 30.0	47.0 ; 47.0	15.0 ; 41.0	15.0 ; 47.0
Height (m)					
N	1	1	1	3	6
Median	1.5	1.6	1.5	1.6	1.6
P25 ; P75	1.5 ; 1.5	1.6 ; 1.6	1.5 ; 1.5	1.6 ; 1.7	1.5 ; 1.6
Mean (SD)	1.5 (.)	1.6 (.)	1.5 (.)	1.6 (0.0)	1.6 (0.1)
Min ; Max	1.5 ; 1.5	1.6 ; 1.6	1.5 ; 1.5	1.6 ; 1.7	1.5 ; 1.7
Body weight (kg)					
N	1	1	1	3	6
Median	45.8	74.4	52.5	55.7	54.6
P25 ; P75	45.8 ; 45.8	74.4 ; 74.4	52.5 ; 52.5	53.4 ; 61.0	52.5 ; 61.0
Mean (SD)	45.8 (.)	74.4 (.)	52.5 (.)	56.7 (3.9)	57.1 (9.8)
Min ; Max	45.8 ; 45.8	74.4 ; 74.4	52.5 ; 52.5	53.4 ; 61.0	45.8 ; 74.4
BMI, (kg/m^2)					
N	1	1	1	3	6
Median	21.5	27.9	22.5	20.5	22.0
P25 ; P75	21.5 ; 21.5	27.9 ; 27.9	22.5 ; 22.5	19.9 ; 24.0	20.5 ; 24.0
Mean (SD)	21.5 (.)	27.9 (.)	22.5 (.)	21.4 (2.2)	22.7 (2.9)
Min ; Max	21.5 ; 21.5	27.9 ; 27.9	22.5 ; 22.5	19.9 ; 24.0	19.9 ; 27.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen.
N: number of subjects, SD: standard deviation, P25/P75 is the 25th/75th percentile, Min: minimum, Max: maximum. Baseline is defined as the latest measurement before first dose with new regimen or before randomisation for arm 1.

3 Bleeding episodes - descriptive statistics - HAwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX				
	Arm 1	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
N in FAS	9	5	18	13	40	71	76
N in FAS and ADS	9	5	18	13	40	71	76
Person years of exposure in ADS	5.4	4.0	15.8	9.5	25.6	50.9	54.8
Weeks of exposure in ADS							
Median	24.0	49.4	48.0	55.9	32.3	34.3	37.0
P25 ; P75	16.1 ; 38.1	32.4 ; 56.1	40.0 ; 55.9	13.3 ; 56.1	32.1 ; 39.8	32.1 ; 48.3	32.1 ; 48.3
Mean (SD)	31.1 (21.8)	41.4 (18.8)	45.8 (10.8)	38.1 (22.8)	33.4 (10.8)	37.4 (14.5)	37.6 (14.7)
Min ; Max	3.9 ; 72.9	12.6 ; 56.3	14.9 ; 56.3	3.6 ; 56.9	2.0 ; 56.1	2.0 ; 56.9	2.0 ; 56.9
Treated spontaneous and traumatic bleeding episodes							
Number of episodes	99	12	35	15	66	116	128
ABR							
Median	11.8	3.7	1.6	0.0	0.0	0.0	0.0
P25 ; P75	7.9 ; 30.8	2.8 ; 4.2	0.0 ; 3.9	0.0 ; 0.9	0.0 ; 4.0	0.0 ; 3.3	0.0 ; 3.7
Mean (SD)	29.2 (32.8)	3.0 (1.8)	2.2 (2.2)	1.1 (1.8)	2.5 (6.0)	2.2 (4.7)	2.2 (4.6)
Min ; Max	5.0 ; 94.7	0.0 ; 4.2	0.0 ; 6.6	0.0 ; 5.6	0.0 ; 35.2	0.0 ; 35.2	0.0 ; 35.2
Treated spontaneous bleeding episodes							
Number of episodes	73	5	16	8	52	76	81
ABR							
Median	10.8	1.1	1.0	0.0	0.0	0.0	0.0
P25 ; P75	6.5 ; 25.2	0.0 ; 1.9	0.0 ; 1.3	0.0 ; 0.0	0.0 ; 1.6	0.0 ; 1.3	0.0 ; 1.4
Mean (SD)	20.4 (21.3)	1.0 (0.9)	1.0 (1.3)	0.6 (1.4)	2.0 (5.6)	1.5 (4.3)	1.4 (4.2)
Min ; Max	3.6 ; 58.2	0.0 ; 1.9	0.0 ; 4.4	0.0 ; 4.7	0.0 ; 33.9	0.0 ; 33.9	0.0 ; 33.9
Treated spontaneous and traumatic joint bleeding episodes							

HAwI: haemophilia A with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - descriptive statistics - HAwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX				
	Arm 1	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
Number of episodes	79	8	31	9	51	91	99
ABR							
Median	8.7	1.1	1.6	0.0	0.0	0.0	0.0
P25 ; P75	5.7 ; 23.8	0.0 ; 2.8	0.0 ; 3.9	0.0 ; 0.9	0.0 ; 1.6	0.0 ; 1.9	0.0 ; 2.0
Mean (SD)	24.6 (30.3)	1.5 (1.7)	2.0 (2.2)	0.6 (1.3)	2.0 (5.6)	1.7 (4.4)	1.7 (4.2)
Min ; Max	0.0 ; 81.2	0.0 ; 3.7	0.0 ; 6.6	0.0 ; 4.7	0.0 ; 33.9	0.0 ; 33.9	0.0 ; 33.9
Treated spontaneous and traumatic target joint bleeding episodes							
Number of episodes	17	0	5	0	20	25	25
ABR							
Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	6.0 (17.2)	0.0 (0.0)	0.3 (0.7)	0.0 (0.0)	0.8 (3.0)	0.5 (2.3)	0.5 (2.2)
Min ; Max	0.0 ; 51.7	0.0 ; 0.0	0.0 ; 2.8	0.0 ; 0.0	0.0 ; 17.0	0.0 ; 17.0	0.0 ; 17.0
All treated and untreated spontaneous and traumatic bleeding episodes							
Number of episodes	103	12	99	16	101	216	228
ABR							
Median	13.7	3.7	3.9	0.0	1.9	1.9	2.2
P25 ; P75	7.9 ; 33.6	2.8 ; 4.2	1.9 ; 6.5	0.0 ; 1.8	0.0 ; 4.8	0.0 ; 4.9	0.0 ; 4.5
Mean (SD)	29.7 (32.7)	3.0 (1.8)	6.3 (10.9)	1.1 (1.8)	3.8 (6.4)	3.9 (7.4)	3.9 (7.2)
Min ; Max	5.0 ; 94.7	0.0 ; 4.2	0.0 ; 48.6	0.0 ; 5.6	0.0 ; 35.2	0.0 ; 48.6	0.0 ; 48.6

HAwI: haemophilia A with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

4 Bleeding episodes - descriptive statistics - HBwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX				
	Arm 1	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
N in FAS	10	8	15	8	20	43	51
N in FAS and ADS	10	8	15	8	20	43	51
Person years of exposure in ADS	6.2	5.4	8.4	8.4	15.8	32.6	37.9
Weeks of exposure in ADS							
Median	34.3	44.0	32.3	63.4	40.7	40.1	40.1
P25 ; P75	24.1 ; 43.9	10.6 ; 55.9	7.9 ; 40.1	51.7 ; 63.9	32.4 ; 56.0	32.1 ; 56.0	31.9 ; 56.0
Mean (SD)	32.6 (15.6)	35.1 (24.0)	29.4 (16.0)	54.6 (17.2)	41.1 (17.3)	39.5 (18.8)	38.8 (19.5)
Min ; Max	4.1 ; 54.1	3.0 ; 56.6	3.1 ; 55.9	14.4 ; 64.1	2.6 ; 64.4	2.6 ; 64.4	2.6 ; 64.4
Treated spontaneous and traumatic bleeding episodes							
Number of episodes	67	10	24	32	86	142	152
ABR							
Median	8.5	0.9	0.0	2.4	1.6	0.0	0.0
P25 ; P75	3.2 ; 14.3	0.0 ; 2.9	0.0 ; 0.0	0.4 ; 5.6	0.0 ; 3.6	0.0 ; 3.3	0.0 ; 3.3
Mean (SD)	8.7 (6.7)	1.5 (1.9)	5.7 (17.3)	3.8 (4.5)	4.5 (10.6)	4.8 (12.4)	4.3 (11.5)
Min ; Max	0.0 ; 20.2	0.0 ; 4.7	0.0 ; 66.4	0.0 ; 13.2	0.0 ; 47.5	0.0 ; 66.4	0.0 ; 66.4
Treated spontaneous bleeding episodes							
Number of episodes	50	5	24	11	60	95	100
ABR							
Median	6.8	0.0	0.0	1.2	0.5	0.0	0.0
P25 ; P75	3.2 ; 8.6	0.0 ; 1.9	0.0 ; 0.0	0.4 ; 2.6	0.0 ; 2.5	0.0 ; 2.4	0.0 ; 2.2
Mean (SD)	6.9 (5.6)	1.0 (1.5)	5.7 (17.3)	1.5 (1.5)	3.2 (7.7)	3.8 (11.4)	3.3 (10.5)
Min ; Max	0.0 ; 16.7	0.0 ; 3.9	0.0 ; 66.4	0.0 ; 3.8	0.0 ; 34.5	0.0 ; 66.4	0.0 ; 66.4
Treated spontaneous and traumatic joint bleeding episodes							

HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - descriptive statistics - HBwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX					
	Arm 1	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
Number of episodes	45	10	16	14	65	95	105
ABR							
Median	6.4	0.9	0.0	1.6	1.1	0.0	0.0
P25 ; P75	2.9 ; 9.8	0.0 ; 2.9	0.0 ; 0.0	0.0 ; 3.0	0.0 ; 3.0	0.0 ; 2.6	0.0 ; 2.6
Mean (SD)	6.2 (4.6)	1.5 (1.9)	5.2 (17.1)	1.9 (2.1)	3.2 (7.4)	3.6 (11.2)	3.3 (10.3)
Min ; Max	0.0 ; 13.1	0.0 ; 4.7	0.0 ; 66.4	0.0 ; 5.7	0.0 ; 33.5	0.0 ; 66.4	0.0 ; 66.4
Treated spontaneous and traumatic target joint bleeding episodes							
Number of episodes	11	1	7	3	40	50	51
ABR							
Median	0.7	0.0	0.0	0.0	0.0	0.0	0.0
P25 ; P75	0.0 ; 2.6	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.5	0.0 ; 1.6	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	1.7 (2.3)	0.1 (0.3)	3.6 (12.8)	0.3 (0.6)	1.9 (4.9)	2.2 (8.2)	1.9 (7.5)
Min ; Max	0.0 ; 6.5	0.0 ; 0.9	0.0 ; 49.8	0.0 ; 1.6	0.0 ; 21.4	0.0 ; 49.8	0.0 ; 49.8
All treated and untreated spontaneous and traumatic bleeding episodes							
Number of episodes	78	11	37	42	108	187	198
ABR							
Median	10.4	0.9	0.0	4.7	2.7	2.5	2.2
P25 ; P75	3.2 ; 15.6	0.0 ; 2.9	0.0 ; 5.0	1.5 ; 6.6	0.0 ; 8.4	0.0 ; 7.6	0.0 ; 5.7
Mean (SD)	10.2 (7.6)	1.7 (2.1)	8.0 (21.3)	4.8 (4.2)	5.7 (10.5)	6.3 (14.4)	5.6 (13.3)
Min ; Max	0.0 ; 20.2	0.0 ; 5.6	0.0 ; 83.0	0.0 ; 13.2	0.0 ; 47.5	0.0 ; 83.0	0.0 ; 83.0

HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

5 Bleeding episodes - zero bleeds during the first 24 weeks of treatment - summary - HAwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX			
	(Arm 1) N (%)	(Arm 2) N (%)	(Arm 3) N (%)	(Arm 4) N (%)	(Arms 2-4) N (%)
N in FAS	9	18	13	40	71
N in FAS and ADS	9(100)	18(100)	13(100)	40(100)	71(100)
Zero Treated spontaneous and traumatic bleeds					
Yes and no permanent treatment discontinuation before week 24	0	8(44.4)	4(30.8)	23(57.5)	35(49.3)
Yes and permanent treatment discontinuation before week 24	0	1(5.6)	5(38.5)	3(7.5)	9(12.7)
No	9(100.0)	9(50.0)	4(30.8)	14(35.0)	27(38.0)
Zero Treated spontaneous bleeds					
Yes and no permanent treatment discontinuation before week 24	0	9(50.0)	6(46.2)	25(62.5)	40(56.3)
Yes and permanent treatment discontinuation before week 24	0	1(5.6)	5(38.5)	3(7.5)	9(12.7)
No	9(100.0)	8(44.4)	2(15.4)	12(30.0)	22(31.0)
Zero Treated spontaneous and traumatic joint bleeds					
Yes and no permanent treatment discontinuation before week 24	0	9(50.0)	6(46.2)	25(62.5)	40(56.3)
Yes and permanent treatment discontinuation before week 24	1(11.1)	1(5.6)	5(38.5)	3(7.5)	9(12.7)
No	8(88.9)	8(44.4)	2(15.4)	12(30.0)	22(31.0)
Zero Treated spontaneous and traumatic target joint bleeds					
Yes and no permanent treatment discontinuation before week 24	5(55.6)	15(83.3)	8(61.5)	31(77.5)	54(76.1)
Yes and permanent treatment discontinuation before week 24	2(22.2)	1(5.6)	5(38.5)	3(7.5)	9(12.7)
No	2(22.2)	2(11.1)	0	6(15.0)	8(11.3)
Zero treated and untreated spontaneous and traumatic bleeds					
Yes and no permanent treatment discontinuation before week 24	0	4(22.2)	4(30.8)	14(35.0)	22(31.0)
Yes and permanent treatment discontinuation before week 24	0	0	5(38.5)	2(5.0)	7(9.9)
No	9(100.0)	14(77.8)	4(30.8)	24(60.0)	42(59.2)

HAwI: haemophilia A with inhibitors, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

6 Bleeding episodes - zero bleeds during the first 24 weeks of treatment - summary - HBwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX			
	(Arm 1) N (%)	(Arm 2) N (%)	(Arm 3) N (%)	(Arm 4) N (%)	(Arms 2-4) N (%)
N in FAS	10	15	8	20	43
N in FAS and ADS	10(100)	15(100)	8(100)	20(100)	43(100)
Zero Treated spontaneous and traumatic bleeds					
Yes and no permanent treatment discontinuation before week 24	1(10.0)	9(60.0)	3(37.5)	7(35.0)	19(44.2)
Yes and permanent treatment discontinuation before week 24	1(10.0)	3(20.0)	0	2(10.0)	5(11.6)
No	8(80.0)	3(20.0)	5(62.5)	11(55.0)	19(44.2)
Zero Treated spontaneous bleeds					
Yes and no permanent treatment discontinuation before week 24	1(10.0)	9(60.0)	4(50.0)	10(50.0)	23(53.5)
Yes and permanent treatment discontinuation before week 24	1(10.0)	3(20.0)	0	2(10.0)	5(11.6)
No	8(80.0)	3(20.0)	4(50.0)	8(40.0)	15(34.9)
Zero Treated spontaneous and traumatic joint bleeds					
Yes and no permanent treatment discontinuation before week 24	2(20.0)	9(60.0)	4(50.0)	7(35.0)	20(46.5)
Yes and permanent treatment discontinuation before week 24	1(10.0)	3(20.0)	0	3(15.0)	6(14.0)
No	7(70.0)	3(20.0)	4(50.0)	10(50.0)	17(39.5)
Zero Treated spontaneous and traumatic target joint bleeds					
Yes and no permanent treatment discontinuation before week 24	3(30.0)	10(66.7)	6(75.0)	11(55.0)	27(62.8)
Yes and permanent treatment discontinuation before week 24	2(20.0)	3(20.0)	1(12.5)	3(15.0)	7(16.3)
No	5(50.0)	2(13.3)	1(12.5)	6(30.0)	9(20.9)
Zero treated and untreated spontaneous and traumatic bleeds					
Yes and no permanent treatment discontinuation before week 24	1(10.0)	7(46.7)	1(12.5)	5(25.0)	13(30.2)
Yes and permanent treatment discontinuation before week 24	1(10.0)	3(20.0)	0	2(10.0)	5(11.6)
No	8(80.0)	5(33.3)	7(87.5)	13(65.0)	25(58.1)

HBwI: haemophilia B with inhibitors, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

7 Bleeding episodes - all treated - by age group - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	Adolescents N (%)	E [%]	Adults N (%)	E [%]
N in FAS	42		85	
N in FAS and ADS	42 (100)		85 (100)	
Treated bleeding episodes	20 (47.6)	61 [100]	42 (49.4)	222 [100]
Cause of bleeding episodes				
Spontaneous	16 (38.1)	32 [52.5]	35 (41.2)	149 [67.1]
Traumatic	11 (26.2)	26 [42.6]	28 (32.9)	72 [32.4]
Surgical	1 (2.4)	2 [3.3]	1 (1.2)	1 [0.5]
Missing	1 (2.4)	1 [1.6]	0	
Location of bleeds				
Treated bleeds	20 (47.6)	64 [100]	42 (49.4)	237 [100]
Joint	19 (45.2)	53 [82.8]	34 (40.0)	164 [69.2]
Target joint	8 (19.0)	17 [26.6]	12 (14.1)	61 [25.7]
Muscular	4 (9.5)	4 [6.3]	19 (22.4)	51 [21.5]
Skin	3 (7.1)	3 [4.7]	7 (8.2)	10 [4.2]
Gastrointestinal or Stomach/gut	1 (2.4)	1 [1.6]	1 (1.2)	7 [3.0]
Mouth, gums or nose	2 (4.8)	3 [4.7]	1 (1.2)	1 [0.4]
Urinary system	0		2 (2.4)	2 [0.8]
Central nervous system	0		0	
Other	0		2 (2.4)	2 [0.8]
Classification of bleeding episodes				
Mild/moderate	17 (40.5)	45 [73.8]	40 (47.1)	208 [93.7]
Severe	7 (16.7)	16 [26.2]	11 (12.9)	14 [6.3]
Location of severe bleeds				
Joint	7 (16.7)	15 [23.4]	5 (5.9)	7 [3.0]
Target joint	4 (9.5)	7 [10.9]	1 (1.2)	2 [0.8]
Muscular	1 (2.4)	1 [1.6]	6 (7.1)	7 [3.0]
Skin	1 (2.4)	1 [1.6]	0	
Gastrointestinal or Stomach/gut	1 (2.4)	1 [1.6]	0	
Mouth, gums or nose	0		0	
Urinary system	0		1 (1.2)	1 [0.4]
Central nervous system	0		0	
Other	0		0	
Pain experience				
Yes	9 (21.4)	14 [23.0]	14 (16.5)	29 [13.1]
No	17 (40.5)	47 [77.0]	33 (38.8)	193 [86.9]
Pain intensity for bleeding episodes with experienced pain				
1	0		0	
2	0		2 (2.4)	4 [1.8]
3	1 (2.4)	1 [1.6]	2 (2.4)	2 [0.9]
4	3 (7.1)	3 [4.9]	0	
5	1 (2.4)	3 [4.9]	6 (7.1)	9 [4.1]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

Bleeding episodes - all treated - by age group - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	Adolescents		Adults	
	N (%)	E [%]	N (%)	E [%]
6	3 (7.1)	3 [4.9]	4 (4.7)	4 [1.8]
7	2 (4.8)	2 [3.3]	2 (2.4)	2 [0.9]
8	1 (2.4)	1 [1.6]	3 (3.5)	5 [2.3]
9	0		2 (2.4)	2 [0.9]
10 (pain as bad as you can imagine)	1 (2.4)	1 [1.6]	1 (1.2)	1 [0.5]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

8 Bleeding episodes - by age group - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	42	85
N in FAS and ADS	42	85
Person years of exposure in ADS	31.6	61.2
Weeks of exposure in ADS		
Median	40.1	39.7
P25 ; P75	32.1 ; 48.4	32.1 ; 55.9
Mean (SD)	39.2 (15.3)	37.6 (17.4)
Min ; Max	2.6 ; 64.4	2.0 ; 64.1
Primary endpoint:		
Treated spontaneous and traumatic bleeding episodes		
Number of episodes	59	221
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 2.6	0.0 ; 3.9
Mean (SD)	1.5 (2.1)	3.8 (9.7)
Min ; Max	0.0 ; 8.1	0.0 ; 66.4
Treated spontaneous bleeding episodes		
Number of episodes	32	149
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 1.6	0.0 ; 1.6
Mean (SD)	0.8 (1.3)	2.9 (9.0)
Min ; Max	0.0 ; 5.7	0.0 ; 66.4
Treated spontaneous and traumatic joint bleeding episodes		
Number of episodes	51	153
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 2.2	0.0 ; 2.5
Mean (SD)	1.3 (1.8)	2.9 (8.8)
Min ; Max	0.0 ; 6.6	0.0 ; 66.4
Treated spontaneous and traumatic target joint bleeding episodes		
Number of episodes	17	59
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	0.4 (1.1)	1.4 (6.2)
Min ; Max	0.0 ; 5.7	0.0 ; 49.8
All treated and untreated spontaneous and traumatic bleeding episodes		
Number of episodes	116	310
ABR		
Median	2.6	1.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - by age group - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
P25 ; P75	0.0 ; 5.0	0.0 ; 4.9
Mean (SD)	3.3 (3.5)	5.2 (12.0)
Min ; Max	0.0 ; 16.2	0.0 ; 83.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

9 Haemostatic medication - consumption to treat bleeding episodes - by age group - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	42	85
N in FAS and ADS	42	85
PYE in ADS	31.6	61.2
N with a treated bleed	20	42
Number of treated bleeds	61	222
FVIII in IU/kg		
N(%) using product	2 (10.0)	4 (9.5)
Number of treated bleeds	2	7
Mean (SD)(consumption per year)	15.6 (1.0)	1788.6 (3136.9)
Mean (SD)(consumption per bleed)	13.0 (4.2)	609.6 (993.4)
Mean (SD)(consumption per injection)	13.0 (4.2)	474.1 (660.8)
Min; Max (consumption per injection)	10.0 ; 16.0	20.0 ; 1500.0
rFVIIa in ug/kg		
N(%) using product	18 (90.0)	37 (88.1)
Number of treated bleeds	57	195
Mean (SD)(consumption per year)	347.8 (439.1)	2963.7 (6448.6)
Mean (SD)(consumption per bleed)	115.6 (166.3)	315.0 (464.7)
Mean (SD)(consumption per injection)	67.9 (53.7)	85.1 (66.1)
Min; Max (consumption per injection)	0.1 ; 267.0	0.1 ; 859.0
FVIIa+FX in ug/kg		
N(%) using product	0	1 (2.4)
Number of treated bleeds	0	1
Mean (SD)(consumption per year)	0	149.5
Mean (SD)(consumption per bleed)	0	160.0
Mean (SD)(consumption per injection)	0	40.0 (23.1)
Min; Max (consumption per injection)	0	20.0 ; 60.0
aPCC in IU/kg		
N(%) using product	1 (5.0)	5 (11.9)
Number of treated bleeds	3	26
Mean (SD)(consumption per year)	12986.7	1243.9 (2243.6)
Mean (SD)(consumption per bleed)	2666.7 (577.4)	180.2 (90.8)
Mean (SD)(consumption per injection)	2666.7 (577.4)	42.6 (11.6)
Min; Max (consumption per injection)	2000.0 ; 3000.0	10.0 ; 80.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure, SD: standard deviation, Min: minimum, Max: maximum.

10 Haemostatic medication - injections to treat bleeding episodes - by age group - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	42	85
N in FAS and ADS	42	85
PYE in ADS	31.6	61.2
N with a treated bleed	20	42
Number of treated bleeds	61	222
Number(%) of injections to treat the bleed		
Using FVIII		
Number of bleeds	2 (100.0)	7 (100.0)
1 injection	2 (100.0)	5 (71.4)
2 injections	0 (0.0)	2 (28.6)
>=3 injection	0 (0.0)	0 (0.0)
Using rFVIIa		
Number of bleeds	57 (100.0)	195 (100.0)
1 injection	36 (63.2)	95 (48.7)
2 injections	11 (19.3)	39 (20.0)
>=3 injection	10 (17.5)	61 (31.3)
Using FVIIa+FX		
Number of bleeds	0	1 (100.0)
1 injection	0	0 (0.0)
2 injections	0	0 (0.0)
>=3 injection	0	1 (100.0)
Using aPCC		
Number of bleeds	3 (100.0)	26 (100.0)
1 injection	3 (100.0)	3 (11.5)
2 injections	0 (0.0)	5 (19.2)
>=3 injection	0 (0.0)	18 (69.2)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure.

11 Haemostatic medication - injections to treat severe bleeding episodes - by age group - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	42	85
N in FAS and ADS	42	85
PYE in ADS	31.6	61.2
N with a treated bleed	7	11
Number of treated bleeds	16	14
Number(%) of injections to treat the bleed		
Using FVIII		
Number of bleeds	0	2 (100.0)
1 injection	0	1 (50.0)
2 injections	0	1 (50.0)
>=3 injection	0	0 (0.0)
Using rFVIIa		
Number of bleeds	16 (100.0)	13 (100.0)
1 injection	12 (75.0)	7 (53.8)
2 injections	3 (18.8)	1 (7.7)
>=3 injection	1 (6.3)	5 (38.5)
Using FVIIa+FX		
Number of bleeds	0	1 (100.0)
1 injection	0	0 (0.0)
2 injections	0	0 (0.0)
>=3 injection	0	1 (100.0)
Using aPCC		
Number of bleeds	0	1 (100.0)
1 injection	0	0 (0.0)
2 injections	0	1 (100.0)
>=3 injection	0	0 (0.0)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure.

12 Haemostatic medication - injections to treat mild or moderate bleeding episodes - by age group - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	42	85
N in FAS and ADS	42	85
PYE in ADS	31.6	61.2
N with a treated bleed	17	40
Number of treated bleeds	45	208
Number(%) of injections to treat the bleed		
Using FVIII		
Number of bleeds	2 (100.0)	5 (100.0)
1 injection	2 (100.0)	4 (80.0)
2 injections	0 (0.0)	1 (20.0)
>=3 injection	0 (0.0)	0 (0.0)
Using rFVIIa		
Number of bleeds	41 (100.0)	182 (100.0)
1 injection	24 (58.5)	88 (48.4)
2 injections	8 (19.5)	38 (20.9)
>=3 injection	9 (22.0)	56 (30.8)
Using aPCC		
Number of bleeds	3 (100.0)	25 (100.0)
1 injection	3 (100.0)	3 (12.0)
2 injections	0 (0.0)	4 (16.0)
>=3 injection	0 (0.0)	18 (72.0)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure.

13 Bleeding episodes - all treated - by race - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)							
	Asian		Black or African American		White		Other	
	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]
N in FAS	34		9		76		8	
N in FAS and ADS	34 (100)		9 (100)		76 (100)		8 (100)	
Treated bleeding episodes	22 (64.7)	79 [100]	4 (44.4)	9 [100]	36 (47.4)	195 [100]	0	
Cause of bleeding episodes								
Spontaneous	18 (52.9)	53 [67.1]	3 (33.3)	5 [55.6]	30 (39.5)	123 [63.1]	0	
Traumatic	12 (35.3)	26 [32.9]	2 (22.2)	3 [33.3]	25 (32.9)	69 [35.4]	0	
Surgical	0		0		2 (2.6)	3 [1.5]	0	
Missing	0		1 (11.1)	1 [11.1]	0		0	
Location of bleeds								
Treated bleeds	22 (64.7)	83 [100]	4 (44.4)	12 [100]	36 (47.4)	206 [100]	0	
Joint	18 (52.9)	60 [72.3]	4 (44.4)	12 [100]	31 (40.8)	145 [70.4]	0	
Target joint	6 (17.6)	16 [19.3]	1 (11.1)	1 [8.3]	13 (17.1)	61 [29.6]	0	
Muscular	9 (26.5)	12 [14.5]	0		14 (18.4)	43 [20.9]	0	
Skin	1 (2.9)	1 [1.2]	0		9 (11.8)	12 [5.8]	0	
Gastrointestinal or Stomach/gut	2 (5.9)	8 [9.6]	0		0		0	
Mouth, gums or nose	1 (2.9)	1 [1.2]	0		2 (2.6)	3 [1.5]	0	
Urinary system	1 (2.9)	1 [1.2]	0		1 (1.3)	1 [0.5]	0	
Central nervous system	0		0		0		0	
Other	0		0		2 (2.6)	2 [1.0]	0	
Classification of bleeding episodes								
Mild/moderate	20 (58.8)	58 [73.4]	4 (44.4)	9 [100]	33 (43.4)	186 [95.4]	0	
Severe	11 (32.4)	21 [26.6]	0		7 (9.2)	9 [4.6]	0	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
Other race includes 'American Indian or Alaska Native' and 'Not Reported'.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

Bleeding episodes - all treated - by race - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)							
	Asian		Black or African American		White		Other	
	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]	N (%)	E [%]
Location of severe bleeds								
Joint	7 (20.6)	16 [19.3]	0		5 (6.6)	6 [2.9]	0	
Target joint	3 (8.8)	6 [7.2]	0		2 (2.6)	3 [1.5]	0	
Muscular	5 (14.7)	5 [6.0]	0		2 (2.6)	3 [1.5]	0	
Skin	0		0		1 (1.3)	1 [0.5]	0	
Gastrointestinal or Stomach/gut	1 (2.9)	1 [1.2]	0		0		0	
Mouth, gums or nose	0		0		0		0	
Urinary system	1 (2.9)	1 [1.2]	0		0		0	
Central nervous system	0		0		0		0	
Other	0		0		0		0	
Pain experience								
Yes	9 (26.5)	16 [20.3]	2 (22.2)	3 [33.3]	12 (15.8)	24 [12.3]	0	
No	16 (47.1)	63 [79.7]	2 (22.2)	6 [66.7]	32 (42.1)	171 [87.7]	0	
Pain intensity for bleeding episodes with experienced pain								
1	0		0		0		0	
2	1 (2.9)	1 [1.3]	0		1 (1.3)	3 [1.5]	0	
3	1 (2.9)	1 [1.3]	0		2 (2.6)	2 [1.0]	0	
4	3 (8.8)	3 [3.8]	0		0		0	
5	2 (5.9)	4 [5.1]	1 (11.1)	2 [22.2]	4 (5.3)	6 [3.1]	0	
6	2 (5.9)	2 [2.5]	0		5 (6.6)	5 [2.6]	0	
7	2 (5.9)	2 [2.5]	0		2 (2.6)	2 [1.0]	0	
8	2 (5.9)	2 [2.5]	1 (11.1)	1 [11.1]	1 (1.3)	3 [1.5]	0	
9	1 (2.9)	1 [1.3]	0		1 (1.3)	1 [0.5]	0	
10 (pain as bad as you can imagine)	0		0		2 (2.6)	2 [1.0]	0	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
Other race includes 'American Indian or Alaska Native' and 'Not Reported'.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

14 Bleeding episodes - by race - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	Asian	Black or African American	White	Other
N in FAS	34	9	76	8
N in FAS and ADS	34	9	76	8
Person years of exposure in ADS	26.0	6.6	56.1	4.1
Weeks of exposure in ADS				
Median	40.1	33.7	40.1	32.1
P25 ; P75	32.4 ; 55.9	32.1 ; 55.9	32.1 ; 55.6	19.5 ; 32.2
Mean (SD)	39.9 (16.3)	38.3 (16.1)	38.5 (17.1)	26.7 (12.7)
Min ; Max	3.0 ; 64.1	6.7 ; 56.1	2.0 ; 64.4	5.4 ; 40.1
Primary endpoint:				
Treated spontaneous and traumatic bleeding episodes				
Number of episodes	79	9	192	0
ABR				
Median	1.5	0.0	0.0	0.0
P25 ; P75	0.0 ; 3.9	0.0 ; 3.3	0.0 ; 3.7	0.0 ; 0.0
Mean (SD)	2.8 (3.7)	2.0 (2.9)	3.6 (10.1)	0.0 (0.0)
Min ; Max	0.0 ; 16.8	0.0 ; 7.8	0.0 ; 66.4	0.0 ; 0.0
Treated spontaneous bleeding episodes				
Number of episodes	53	5	123	0
ABR				
Median	1.0	0.0	0.0	0.0
P25 ; P75	0.0 ; 2.4	0.0 ; 1.6	0.0 ; 1.6	0.0 ; 0.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate. P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.
Other race includes 'American Indian or Alaska Native' and 'Not Reported'.

Bleeding episodes - by race - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	Asian	Black or African American	White	Other
Mean (SD)	1.9 (3.4)	1.5 (2.7)	2.7 (9.3)	0.0 (0.0)
Min ; Max	0.0 ; 16.8	0.0 ; 7.8	0.0 ; 66.4	0.0 ; 0.0
Treated spontaneous and traumatic joint bleeding episodes				
Number of episodes	58	9	137	0
ABR				
Median	1.1	0.0	0.0	0.0
P25 ; P75	0.0 ; 3.9	0.0 ; 3.3	0.0 ; 2.3	0.0 ; 0.0
Mean (SD)	1.9 (2.5)	2.0 (2.9)	2.8 (9.2)	0.0 (0.0)
Min ; Max	0.0 ; 10.3	0.0 ; 7.8	0.0 ; 66.4	0.0 ; 0.0
Treated spontaneous and traumatic target joint bleeding episodes				
Number of episodes	16	1	59	0
ABR				
Median	0.0	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	0.5 (1.2)	0.9 (2.6)	1.4 (6.5)	0.0 (0.0)
Min ; Max	0.0 ; 4.6	0.0 ; 7.8	0.0 ; 49.8	0.0 ; 0.0
All treated and untreated spontaneous and traumatic bleeding episodes				
Number of episodes	164	13	241	8
ABR				
Median	3.6	1.9	1.9	0.8
P25 ; P75	0.0 ; 7.8	1.5 ; 3.3	0.0 ; 3.9	0.0 ; 2.9
Mean (SD)	5.6 (8.7)	2.6 (2.5)	4.7 (11.6)	1.6 (1.9)
Min ; Max	0.0 ; 48.6	0.0 ; 7.8	0.0 ; 83.0	0.0 ; 5.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate. P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.
Other race includes 'American Indian or Alaska Native' and 'Not Reported'.

15 Bleeding episodes - all treated - by ethnicity - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)		
	Hispanic or Latino N (%) E [%]	Not Hispanic or Latino N (%) E [%]	Not Reported N (%) E [%]
N in FAS	6	117	4
N in FAS and ADS	6 (100)	117 (100)	4 (100)
Treated bleeding episodes	0	62 (53.0) 283 [100]	0
Cause of bleeding episodes			
Spontaneous	0	51 (43.6) 181 [64.0]	0
Traumatic	0	39 (33.3) 98 [34.6]	0
Surgical	0	2 (1.7) 3 [1.1]	0
Missing	0	1 (0.9) 1 [0.4]	0
Location of bleeds			
Treated bleeds	0	62 (53.0) 301 [100]	0
Joint	0	53 (45.3) 217 [72.1]	0
Target joint	0	20 (17.1) 78 [25.9]	0
Muscular	0	23 (19.7) 55 [18.3]	0
Skin	0	10 (8.5) 13 [4.3]	0
Gastrointestinal or Stomach/gut	0	2 (1.7) 8 [2.7]	0
Mouth, gums or nose	0	3 (2.6) 4 [1.3]	0
Urinary system	0	2 (1.7) 2 [0.7]	0
Central nervous system	0	0	0
Other	0	2 (1.7) 2 [0.7]	0
Classification of bleeding episodes			
Mild/moderate	0	57 (48.7) 253 [89.4]	0
Severe	0	18 (15.4) 30 [10.6]	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

Bleeding episodes - all treated - by ethnicity - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)		
	Hispanic or Latino N (%) E [%]	Not Hispanic or Latino N (%) E [%]	Not Reported N (%) E [%]
Location of severe bleeds			
Joint	0	12 (10.3) 22 [7.3]	0
Target joint	0	5 (4.3) 9 [3.0]	0
Muscular	0	7 (6.0) 8 [2.7]	0
Skin	0	1 (0.9) 1 [0.3]	0
Gastrointestinal or Stomach/gut	0	1 (0.9) 1 [0.3]	0
Mouth, gums or nose	0	0	0
Urinary system	0	1 (0.9) 1 [0.3]	0
Central nervous system	0	0	0
Other	0	0	0
Pain experience			
Yes	0	23 (19.7) 43 [15.2]	0
No	0	50 (42.7) 240 [84.8]	0
Pain intensity for bleeding episodes with experienced pain			
1	0	0	0
2	0	2 (1.7) 4 [1.4]	0
3	0	3 (2.6) 3 [1.1]	0
4	0	3 (2.6) 3 [1.1]	0
5	0	7 (6.0) 12 [4.2]	0
6	0	7 (6.0) 7 [2.5]	0
7	0	4 (3.4) 4 [1.4]	0
8	0	4 (3.4) 6 [2.1]	0
9	0	2 (1.7) 2 [0.7]	0
10 (pain as bad as you can imagine)	0	2 (1.7) 2 [0.7]	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

16 Bleeding episodes - by ethnicity - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)		
	Hispanic or Latino	Not Hispanic or Latino	Not Reported
N in FAS	6	117	4
N in FAS and ADS	6	117	4
Person years of exposure in ADS	3.5	87.3	2.0
Weeks of exposure in ADS			
Median	32.1	40.1	32.1
P25 ; P75	31.1 ; 40.1	32.1 ; 55.9	18.8 ; 32.2
Mean (SD)	30.6 (11.9)	38.9 (16.8)	25.5 (13.4)
Min ; Max	7.9 ; 40.4	2.0 ; 64.4	5.4 ; 32.3
Primary endpoint:			
Treated spontaneous and traumatic bleeding episodes			
Number of episodes	0	280	0
ABR			
Median	0.0	0.9	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 3.7	0.0 ; 0.0
Mean (SD)	0.0 (0.0)	3.3 (8.4)	0.0 (0.0)
Min ; Max	0.0 ; 0.0	0.0 ; 66.4	0.0 ; 0.0
Treated spontaneous bleeding episodes			
Number of episodes	0	181	0
ABR			
Median	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 1.8	0.0 ; 0.0
Mean (SD)	0.0 (0.0)	2.4 (7.7)	0.0 (0.0)
Min ; Max	0.0 ; 0.0	0.0 ; 66.4	0.0 ; 0.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate. P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - by ethnicity - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)		
	Hispanic or Latino	Not Hispanic or Latino	Not Reported
Treated spontaneous and traumatic joint bleeding episodes			
Number of episodes	0	204	0
ABR			
Median	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 2.6	0.0 ; 0.0
Mean (SD)	0.0 (0.0)	2.5 (7.6)	0.0 (0.0)
Min ; Max	0.0 ; 0.0	0.0 ; 66.4	0.0 ; 0.0
Treated spontaneous and traumatic target joint bleeding episodes			
Number of episodes	0	76	0
ABR			
Median	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	0.0 (0.0)	1.1 (5.3)	0.0 (0.0)
Min ; Max	0.0 ; 0.0	0.0 ; 49.8	0.0 ; 0.0
All treated and untreated spontaneous and traumatic bleeding episodes			
Number of episodes	7	418	1
ABR			
Median	1.3	2.3	0.0
P25 ; P75	0.0 ; 3.2	0.0 ; 5.3	0.0 ; 0.8
Mean (SD)	1.8 (2.1)	4.9 (10.4)	0.4 (0.8)
Min ; Max	0.0 ; 5.0	0.0 ; 83.0	0.0 ; 1.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate. P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

17 Bleeding episodes - all treated - US vs non-US - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	US		non-US	
	N (%)	E [%]	N (%)	E [%]
N in FAS	6		121	
N in FAS and ADS	6 (100)		121 (100)	
Treated bleeding episodes	1 (16.7)	4 [100]	61 (50.4)	279 [100]
Cause of bleeding episodes				
Spontaneous	1 (16.7)	4 [100]	50 (41.3)	177 [63.4]
Traumatic	0		39 (32.2)	98 [35.1]
Surgical	0		2 (1.7)	3 [1.1]
Missing	0		1 (0.8)	1 [0.4]
Location of bleeds				
Treated bleeds	1 (16.7)	7 [100]	61 (50.4)	294 [100]
Joint	1 (16.7)	7 [100]	52 (43.0)	210 [71.4]
Target joint	1 (16.7)	3 [42.9]	19 (15.7)	75 [25.5]
Muscular	0		23 (19.0)	55 [18.7]
Skin	0		10 (8.3)	13 [4.4]
Gastrointestinal or Stomach/gut	0		2 (1.7)	8 [2.7]
Mouth, gums or nose	0		3 (2.5)	4 [1.4]
Urinary system	0		2 (1.7)	2 [0.7]
Central nervous system	0		0	
Other	0		2 (1.7)	2 [0.7]
Classification of bleeding episodes				
Mild/moderate	1 (16.7)	4 [100]	56 (46.3)	249 [89.2]
Severe	0		18 (14.9)	30 [10.8]
Location of severe bleeds				
Joint	0		12 (9.9)	22 [7.5]
Target joint	0		5 (4.1)	9 [3.1]
Muscular	0		7 (5.8)	8 [2.7]
Skin	0		1 (0.8)	1 [0.3]
Gastrointestinal or Stomach/gut	0		1 (0.8)	1 [0.3]
Mouth, gums or nose	0		0	
Urinary system	0		1 (0.8)	1 [0.3]
Central nervous system	0		0	
Other	0		0	
Pain experience				
Yes	1 (16.7)	4 [100]	22 (18.2)	39 [14.0]
No	0		50 (41.3)	240 [86.0]
Pain intensity for bleeding episodes with experienced pain				
1	0		0	
2	0		2 (1.7)	4 [1.4]
3	0		3 (2.5)	3 [1.1]
4	0		3 (2.5)	3 [1.1]
5	0		7 (5.8)	12 [4.3]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis.
N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

Bleeding episodes - all treated - US vs non-US - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)			
	US		non-US	
	N (%)	E [%]	N (%)	E [%]
6	0		7 (5.8)	7 [2.5]
7	1 (16.7)	1 [25.0]	3 (2.5)	3 [1.1]
8	1 (16.7)	3 [75.0]	3 (2.5)	3 [1.1]
9	0		2 (1.7)	2 [0.7]
10 (pain as bad as you can imagine)	0		2 (1.7)	2 [0.7]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis.
N: number of subjects, (%): percentage of subjects, E: number of bleeding episodes, [%]: percentage of bleeding episodes, FAS: Full analysis set, ADS: Analysis data set.
Bleeding episodes with multiple locations are counted in all these locations.
For location of bleeds the E represents the number of bleeds and [%] is the percentage of bleeds.

18 Bleeding episodes - US vs non-US - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	US	non-US
N in FAS	6	121
N in FAS and ADS	6	121
Person years of exposure in ADS	3.8	89.0
Weeks of exposure in ADS		
Median	36.3	40.0
P25 ; P75	32.1 ; 40.4	32.1 ; 55.9
Mean (SD)	32.7 (15.7)	38.4 (16.8)
Min ; Max	3.1 ; 48.1	2.0 ; 64.4
Primary endpoint:		
Treated spontaneous and traumatic bleeding episodes		
Number of episodes	4	276
ABR		
Median	0.0	0.8
P25 ; P75	0.0 ; 0.0	0.0 ; 3.6
Mean (SD)	11.1 (27.1)	2.7 (5.9)
Min ; Max	0.0 ; 66.4	0.0 ; 47.5
Treated spontaneous bleeding episodes		
Number of episodes	4	177
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 1.6
Mean (SD)	11.1 (27.1)	1.8 (4.8)
Min ; Max	0.0 ; 66.4	0.0 ; 34.5
Treated spontaneous and traumatic joint bleeding episodes		
Number of episodes	4	200
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 2.5
Mean (SD)	11.1 (27.1)	1.9 (4.6)
Min ; Max	0.0 ; 66.4	0.0 ; 33.9
Treated spontaneous and traumatic target joint bleeding episodes		
Number of episodes	3	73
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 0.0
Mean (SD)	8.3 (20.3)	0.7 (2.7)
Min ; Max	0.0 ; 49.8	0.0 ; 21.4
All treated and untreated spontaneous and traumatic bleeding episodes		
Number of episodes	7	419
ABR		
Median	0.0	2.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - US vs non-US - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	US	non-US
P25 ; P75	0.0 ; 2.6	0.0 ; 5.0
Mean (SD)	14.3 (33.7)	4.1 (7.4)
Min ; Max	0.0 ; 83.0	0.0 ; 48.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

19 Haemostatic medication - consumption to treat bleeding episodes - US vs non-US - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	US	non-US
N in FAS	6	121
N in FAS and ADS	6	121
PYE in ADS	3.8	89.0
N with a treated bleed	1	61
Number of treated bleeds	4	279
FVIII in IU/kg		
N(%) using product	0	6 (9.8)
Number of treated bleeds	0	9
Mean (SD)(consumption per year)	0	1197.6 (2596.6)
Mean (SD)(consumption per bleed)	0	477.0 (899.7)
Mean (SD)(consumption per injection)	0	390.3 (619.8)
Min; Max (consumption per injection)	0	10.0 ; 1500.0
rFVIIa in ug/kg		
N(%) using product	1 (100.0)	54 (88.5)
Number of treated bleeds	4	248
Mean (SD)(consumption per year)	32673.3	1541.6 (3452.2)
Mean (SD)(consumption per bleed)	492.0 (608.7)	266.3 (421.5)
Mean (SD)(consumption per injection)	109.3 (25.8)	82.5 (65.4)
Min; Max (consumption per injection)	45.0 ; 130.0	0.1 ; 859.0
FVIIa+FX in ug/kg		
N(%) using product	0	1 (1.6)
Number of treated bleeds	0	1
Mean (SD)(consumption per year)	0	149.5
Mean (SD)(consumption per bleed)	0	160.0
Mean (SD)(consumption per injection)	0	40.0 (23.1)
Min; Max (consumption per injection)	0	20.0 ; 60.0
aPCC in IU/kg		
N(%) using product	0	6 (9.8)
Number of treated bleeds	0	29
Mean (SD)(consumption per year)	0	3201.0 (5197.0)
Mean (SD)(consumption per bleed)	0	437.4 (790.6)
Mean (SD)(consumption per injection)	0	112.3 (430.8)
Min; Max (consumption per injection)	0	10.0 ; 3000.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure, SD: standard deviation, Min: minimum, Max: maximum.

20 Haemostatic medication - injections to treat bleeding episodes - US vs non-US - summary - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	US	non-US
N in FAS	6	121
N in FAS and ADS	6	121
PYE in ADS	3.8	89.0
N with a treated bleed	1	61
Number of treated bleeds	4	279
Number(%) of injections to treat the bleed		
Using FVIII		
Number of bleeds	0	9 (100.0)
1 injection	0	7 (77.8)
2 injections	0	2 (22.2)
>=3 injection	0	0 (0.0)
Using rFVIIa		
Number of bleeds	4 (100.0)	248 (100.0)
1 injection	2 (50.0)	129 (52.0)
2 injections	0 (0.0)	50 (20.2)
>=3 injection	2 (50.0)	69 (27.8)
Using FVIIa+FX		
Number of bleeds	0	1 (100.0)
1 injection	0	0 (0.0)
2 injections	0	0 (0.0)
>=3 injection	0	1 (100.0)
Using aPCC		
Number of bleeds	0	29 (100.0)
1 injection	0	6 (20.7)
2 injections	0	5 (17.2)
>=3 injection	0	18 (62.1)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, PYE: patient years of exposure.

21 SF-36v2 (standard version) - bodily pain - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	46.3	42.2
P25 ; P75	38.2 ; 55.6	34.6 ; 51.5
Mean (SD)	46.7 (8.7)	42.7 (10.1)
Min ; Max	38.2 ; 55.6	21.7 ; 62.0
Week 24		
N	5	85
Median	53.9	50.7
P25 ; P75	42.2 ; 62.0	43.5 ; 62.0
Mean (SD)	51.0 (12.2)	51.1 (9.3)
Min ; Max	34.6 ; 62.0	30.6 ; 62.0
Week 32		
N	5	83
Median	46.7	51.5
P25 ; P75	42.2 ; 62.0	42.6 ; 62.0
Mean (SD)	50.2 (11.2)	50.3 (10.3)
Min ; Max	38.2 ; 62.0	25.7 ; 62.0
Change from baseline to week 24		
N	3	63
Median	6.5	4.8
P25 ; P75	-3.6 ; 15.7	0.0 ; 12.5
Mean (SD)	6.2 (9.7)	7.0 (9.8)
Min ; Max	-3.6 ; 15.7	-13.3 ; 29.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

22 SF-36v2 (standard version) - physical functioning - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	49.9	40.3
P25 ; P75	34.6 ; 53.7	30.8 ; 48.0
Mean (SD)	46.1 (10.1)	38.9 (11.0)
Min ; Max	34.6 ; 53.7	19.3 ; 57.5
Week 24		
N	5	85
Median	46.1	48.0
P25 ; P75	38.4 ; 55.6	38.4 ; 53.7
Mean (SD)	46.8 (9.6)	44.8 (10.8)
Min ; Max	36.5 ; 57.5	21.2 ; 57.5
Week 32		
N	5	83
Median	36.5	48.0
P25 ; P75	36.5 ; 49.9	36.5 ; 53.7
Mean (SD)	43.0 (10.2)	44.5 (11.1)
Min ; Max	34.6 ; 57.5	19.3 ; 57.5
Change from baseline to week 24		
N	3	63
Median	3.8	3.8
P25 ; P75	1.9 ; 5.8	0.0 ; 7.7
Mean (SD)	3.8 (1.9)	4.1 (7.1)
Min ; Max	1.9 ; 5.8	-15.3 ; 30.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

23 SF-36v2 (standard version) - Role - Physical - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	50.4	41.4
P25 ; P75	34.7 ; 57.2	34.7 ; 45.9
Mean (SD)	47.4 (11.5)	40.5 (9.4)
Min ; Max	34.7 ; 57.2	21.2 ; 57.2
Week 24		
N	5	85
Median	50.4	48.2
P25 ; P75	48.2 ; 54.9	41.4 ; 54.9
Mean (SD)	50.0 (7.0)	47.5 (8.0)
Min ; Max	39.2 ; 57.2	21.2 ; 57.2
Week 32		
N	5	83
Median	45.9	48.2
P25 ; P75	43.7 ; 48.2	41.4 ; 57.2
Mean (SD)	46.8 (6.7)	47.0 (9.3)
Min ; Max	39.2 ; 57.2	21.2 ; 57.2
Change from baseline to week 24		
N	3	63
Median	4.5	4.5
P25 ; P75	0.0 ; 4.5	0.0 ; 13.5
Mean (SD)	3.0 (2.6)	5.6 (9.6)
Min ; Max	0.0 ; 4.5	-18.0 ; 26.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

24 SF-36v2 (standard version) - General Health - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	53.2	43.7
P25 ; P75	46.1 ; 53.2	35.6 ; 48.4
Mean (SD)	50.8 (4.1)	41.7 (10.3)
Min ; Max	46.1 ; 53.2	21.3 ; 66.5
Week 24		
N	5	85
Median	53.2	48.4
P25 ; P75	50.8 ; 55.6	41.3 ; 55.6
Mean (SD)	52.5 (5.9)	48.6 (9.6)
Min ; Max	43.7 ; 59.4	26.1 ; 66.5
Week 32		
N	5	83
Median	52.2	50.8
P25 ; P75	50.8 ; 52.2	41.3 ; 57.0
Mean (SD)	51.9 (5.9)	48.7 (10.6)
Min ; Max	43.7 ; 60.3	26.1 ; 66.5
Change from baseline to week 24		
N	3	63
Median	0.0	4.8
P25 ; P75	-2.4 ; 6.2	0.0 ; 12.8
Mean (SD)	1.3 (4.4)	6.0 (10.5)
Min ; Max	-2.4 ; 6.2	-13.3 ; 34.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

25 SF-36v2 (standard version) - Vitality - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	43.7	49.6
P25 ; P75	37.7 ; 61.5	40.7 ; 55.6
Mean (SD)	47.6 (12.4)	47.7 (9.6)
Min ; Max	37.7 ; 61.5	22.9 ; 70.4
Week 24		
N	5	85
Median	55.6	55.6
P25 ; P75	52.6 ; 55.6	49.6 ; 61.5
Mean (SD)	53.8 (4.5)	54.4 (7.9)
Min ; Max	46.7 ; 58.5	37.7 ; 70.4
Week 32		
N	5	83
Median	46.7	55.6
P25 ; P75	43.7 ; 61.5	46.7 ; 61.5
Mean (SD)	52.0 (10.2)	53.5 (9.4)
Min ; Max	43.7 ; 64.5	28.8 ; 70.4
Change from baseline to week 24		
N	3	63
Median	8.9	5.9
P25 ; P75	-5.9 ; 14.9	0.0 ; 11.9
Mean (SD)	5.9 (10.7)	6.5 (10.3)
Min ; Max	-5.9 ; 14.9	-26.7 ; 41.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

26 SF-36v2 (standard version) - Social Functioning - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	57.3	42.3
P25 ; P75	47.3 ; 57.3	37.3 ; 49.8
Mean (SD)	54.0 (5.8)	42.0 (10.8)
Min ; Max	47.3 ; 57.3	17.2 ; 57.3
Week 24		
N	5	85
Median	47.3	52.3
P25 ; P75	47.3 ; 57.3	42.3 ; 57.3
Mean (SD)	51.3 (5.5)	49.4 (8.6)
Min ; Max	47.3 ; 57.3	17.2 ; 57.3
Week 32		
N	5	83
Median	47.3	47.3
P25 ; P75	47.3 ; 52.3	37.3 ; 57.3
Mean (SD)	50.3 (4.5)	48.0 (10.4)
Min ; Max	47.3 ; 57.3	17.2 ; 57.3
Change from baseline to week 24		
N	3	63
Median	0.0	5.0
P25 ; P75	-10.0 ; 0.0	0.0 ; 10.0
Mean (SD)	-3.3 (5.8)	6.4 (10.8)
Min ; Max	-10.0 ; 0.0	-15.0 ; 40.1

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

27 SF-36v2 (standard version) - Role - Emotional - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	52.7	45.7
P25 ; P75	49.2 ; 56.2	35.3 ; 56.2
Mean (SD)	52.7 (3.5)	43.7 (11.0)
Min ; Max	49.2 ; 56.2	14.4 ; 56.2
Week 24		
N	5	85
Median	56.2	49.2
P25 ; P75	56.2 ; 56.2	42.2 ; 56.2
Mean (SD)	55.5 (1.6)	47.9 (8.8)
Min ; Max	52.7 ; 56.2	14.4 ; 56.2
Week 32		
N	5	83
Median	56.2	45.7
P25 ; P75	56.2 ; 56.2	38.8 ; 56.2
Mean (SD)	55.5 (1.6)	46.1 (10.2)
Min ; Max	52.7 ; 56.2	21.4 ; 56.2
Change from baseline to week 24		
N	3	63
Median	3.5	0.0
P25 ; P75	0.0 ; 7.0	0.0 ; 10.4
Mean (SD)	3.5 (3.5)	4.2 (10.0)
Min ; Max	0.0 ; 7.0	-31.3 ; 31.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

28 SF-36v2 (standard version) - Mental Health - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	53.5	48.3
P25 ; P75	53.5 ; 56.1	39.1 ; 53.5
Mean (SD)	54.4 (1.5)	45.8 (10.3)
Min ; Max	53.5 ; 56.1	19.5 ; 64.0
Week 24		
N	5	85
Median	56.1	50.9
P25 ; P75	56.1 ; 56.1	43.0 ; 56.1
Mean (SD)	56.1 (1.9)	49.9 (8.3)
Min ; Max	53.5 ; 58.7	24.7 ; 64.0
Week 32		
N	5	83
Median	53.5	50.9
P25 ; P75	50.9 ; 53.5	43.0 ; 56.1
Mean (SD)	53.5 (3.2)	49.2 (9.5)
Min ; Max	50.9 ; 58.7	24.7 ; 64.0
Change from baseline to week 24		
N	3	63
Median	2.6	2.6
P25 ; P75	-2.6 ; 2.6	-2.6 ; 10.5
Mean (SD)	0.9 (3.0)	4.3 (11.6)
Min ; Max	-2.6 ; 2.6	-15.7 ; 36.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

29 SF-36v2 (standard version) - Physical health component score - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	48.8	40.3
P25 ; P75	31.7 ; 54.5	34.3 ; 46.7
Mean (SD)	45.0 (11.8)	39.7 (9.1)
Min ; Max	31.7 ; 54.5	19.5 ; 60.2
Week 24		
N	5	85
Median	47.7	48.9
P25 ; P75	40.9 ; 56.9	40.6 ; 54.8
Mean (SD)	47.3 (11.6)	47.5 (9.3)
Min ; Max	31.4 ; 59.5	25.1 ; 66.1
Week 32		
N	5	83
Median	37.8	47.3
P25 ; P75	37.2 ; 51.0	38.6 ; 56.1
Mean (SD)	44.7 (10.9)	47.4 (10.4)
Min ; Max	36.4 ; 61.0	23.2 ; 70.6
Change from baseline to week 24		
N	3	63
Median	5.1	6.1
P25 ; P75	-0.3 ; 8.2	0.7 ; 11.0
Mean (SD)	4.3 (4.3)	5.8 (7.7)
Min ; Max	-0.3 ; 8.2	-9.6 ; 28.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

30 SF-36v2 (standard version) - Mental health component score - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	68
Median	55.9	49.0
P25 ; P75	52.5 ; 57.6	39.3 ; 54.3
Mean (SD)	55.3 (2.6)	47.1 (10.0)
Min ; Max	52.5 ; 57.6	20.1 ; 63.0
Week 24		
N	5	85
Median	56.5	52.5
P25 ; P75	55.7 ; 60.2	46.3 ; 58.1
Mean (SD)	57.2 (3.9)	51.4 (9.1)
Min ; Max	51.8 ; 61.8	29.7 ; 68.4
Week 32		
N	5	83
Median	56.7	52.2
P25 ; P75	56.5 ; 57.2	43.7 ; 58.4
Mean (SD)	56.6 (1.7)	49.9 (10.7)
Min ; Max	53.8 ; 58.7	17.5 ; 69.5
Change from baseline to week 24		
N	3	63
Median	3.2	3.2
P25 ; P75	-5.8 ; 4.3	-2.4 ; 10.1
Mean (SD)	0.6 (5.5)	4.8 (10.9)
Min ; Max	-5.8 ; 4.3	-12.5 ; 37.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

31 PROMIS numeric rating scale v.1.0 - pain intensity 1a - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	65
Median	1.0	3.0
P25 ; P75	1.0 ; 6.0	1.0 ; 5.0
Mean (SD)	2.7 (2.9)	3.5 (2.7)
Min ; Max	1.0 ; 6.0	0.0 ; 10.0
Week 24		
N	5	83
Median	0.0	1.0
P25 ; P75	0.0 ; 4.0	0.0 ; 3.0
Mean (SD)	2.2 (3.2)	2.0 (2.2)
Min ; Max	0.0 ; 7.0	0.0 ; 9.0
Week 32		
N	5	81
Median	0.0	1.0
P25 ; P75	0.0 ; 3.0	0.0 ; 4.0
Mean (SD)	2.2 (3.5)	2.2 (2.6)
Min ; Max	0.0 ; 8.0	0.0 ; 9.0
Change from baseline to week 24		
N	3	59
Median	-1.0	-1.0
P25 ; P75	-2.0 ; -1.0	-2.0 ; 0.0
Mean (SD)	-1.3 (0.6)	-1.1 (2.4)
Min ; Max	-2.0 ; -1.0	-8.0 ; 5.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

32 PROMIS short form v2.0 - upper extremity 7a - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	54
Median	44.8	39.5
P25 ; P75	39.5 ; 58.2	32.5 ; 45.1
Mean (SD)	47.5 (9.6)	39.8 (9.6)
Min ; Max	39.5 ; 58.2	23.0 ; 58.2
Week 24		
N	5	70
Median	44.6	44.6
P25 ; P75	43.4 ; 45.0	37.7 ; 58.2
Mean (SD)	46.0 (7.2)	45.1 (10.2)
Min ; Max	38.9 ; 58.2	24.1 ; 58.2
Week 32		
N	5	69
Median	45.0	46.8
P25 ; P75	41.2 ; 51.4	37.4 ; 58.2
Mean (SD)	47.3 (7.5)	45.9 (10.5)
Min ; Max	40.7 ; 58.2	23.8 ; 58.2
Change from baseline to week 24		
N	3	50
Median	-0.2	1.9
P25 ; P75	-0.5 ; 0.0	-1.2 ; 8.3
Mean (SD)	-0.2 (0.3)	3.4 (7.1)
Min ; Max	-0.5 ; 0.0	-9.7 ; 20.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

33 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Total score - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	55
Median	40.7	40.5
P25 ; P75	39.9 ; 41.5	31.3 ; 62.2
Mean (SD)	40.7 (1.1)	44.2 (17.6)
Min ; Max	39.9 ; 41.5	14.8 ; 82.6
Week 24		
N		40
Median		29.8
P25 ; P75		17.4 ; 42.5
Mean (SD)		30.8 (16.9)
Min ; Max		4.7 ; 62.8
Week 32		
N		36
Median		26.5
P25 ; P75		17.8 ; 41.0
Mean (SD)		30.9 (17.7)
Min ; Max		8.3 ; 84.4
Change from baseline to week 24		
N		39
Median		-7.1
P25 ; P75		-19.3 ; -1.7
Mean (SD)		-12.9 (19.4)
Min ; Max		-57.9 ; 43.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

34 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Physical health - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	55
Median	70.0	55.0
P25 ; P75	60.0 ; 80.0	30.0 ; 75.0
Mean (SD)	70.0 (14.1)	52.7 (26.5)
Min ; Max	60.0 ; 80.0	0.0 ; 95.0
Week 24		
N		40
Median		25.0
P25 ; P75		12.5 ; 55.0
Mean (SD)		32.9 (26.6)
Min ; Max		0.0 ; 95.0
Week 32		
N		35
Median		25.0
P25 ; P75		10.0 ; 45.0
Mean (SD)		29.9 (24.3)
Min ; Max		0.0 ; 85.0
Change from baseline to week 24		
N		39
Median		-25.0
P25 ; P75		-40.0 ; -5.0
Mean (SD)		-19.1 (31.4)
Min ; Max		-75.0 ; 95.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

35 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Feeling - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	55
Median	18.8	31.3
P25 ; P75	12.5 ; 25.0	18.8 ; 62.5
Mean (SD)	18.8 (8.8)	39.3 (27.1)
Min ; Max	12.5 ; 25.0	0.0 ; 100.0
Week 24		
N		40
Median		18.8
P25 ; P75		3.1 ; 37.5
Mean (SD)		24.4 (23.3)
Min ; Max		0.0 ; 87.5
Week 32		
N		35
Median		12.5
P25 ; P75		0.0 ; 37.5
Mean (SD)		21.1 (24.3)
Min ; Max		0.0 ; 93.8
Change from baseline to week 24		
N		39
Median		-12.5
P25 ; P75		-25.0 ; 0.0
Mean (SD)		-16.0 (27.0)
Min ; Max		-87.5 ; 56.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

36 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - View of yourself - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	54
Median	40.0	45.0
P25 ; P75	35.0 ; 45.0	40.0 ; 60.0
Mean (SD)	40.0 (7.1)	49.2 (17.6)
Min ; Max	35.0 ; 45.0	5.0 ; 85.0
Week 24		
N		40
Median		40.0
P25 ; P75		20.0 ; 50.0
Mean (SD)		38.8 (22.0)
Min ; Max		0.0 ; 95.0
Week 32		
N		35
Median		45.0
P25 ; P75		20.0 ; 55.0
Mean (SD)		39.4 (22.6)
Min ; Max		0.0 ; 95.0
Change from baseline to week 24		
N		38
Median		-5.0
P25 ; P75		-20.0 ; 5.0
Mean (SD)		-9.6 (22.3)
Min ; Max		-70.0 ; 30.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

37 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Sport and leisure - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	45
Median	90.0	75.0
P25 ; P75	90.0 ; 90.0	60.0 ; 85.0
Mean (SD)	90.0 (0.0)	68.9 (22.2)
Min ; Max	90.0 ; 90.0	16.7 ; 100.0
Week 24		
N		33
Median		50.0
P25 ; P75		35.0 ; 80.0
Mean (SD)		52.3 (27.0)
Min ; Max		0.0 ; 100.0
Week 32		
N		28
Median		55.6
P25 ; P75		40.8 ; 75.0
Mean (SD)		57.2 (25.2)
Min ; Max		0.0 ; 100.0
Change from baseline to week 24		
N		27
Median		-8.8
P25 ; P75		-30.0 ; 0.0
Mean (SD)		-14.8 (20.6)
Min ; Max		-62.5 ; 10.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

38 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Work and studies - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N		46
Median		40.6
P25 ; P75		25.0 ; 56.3
Mean (SD)		42.0 (24.6)
Min ; Max		0.0 ; 100.0
Week 24		
N		31
Median		25.0
P25 ; P75		0.0 ; 37.5
Mean (SD)		25.6 (23.6)
Min ; Max		0.0 ; 87.5
Week 32		
N		29
Median		12.5
P25 ; P75		0.0 ; 43.8
Mean (SD)		23.7 (28.0)
Min ; Max		0.0 ; 93.8
Change from baseline to week 24		
N		29
Median		-12.5
P25 ; P75		-33.3 ; 0.0
Mean (SD)		-16.7 (24.3)
Min ; Max		-68.8 ; 25.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

39 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Dealing with haemophilia - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	55
Median	16.7	33.3
P25 ; P75	8.3 ; 25.0	16.7 ; 41.7
Mean (SD)	16.7 (11.8)	30.3 (19.2)
Min ; Max	8.3 ; 25.0	0.0 ; 100.0
Week 24		
N		40
Median		25.0
P25 ; P75		8.3 ; 37.5
Mean (SD)		26.7 (21.3)
Min ; Max		0.0 ; 66.7
Week 32		
N		35
Median		16.7
P25 ; P75		0.0 ; 33.3
Mean (SD)		20.5 (20.2)
Min ; Max		0.0 ; 66.7
Change from baseline to week 24		
N		39
Median		-8.3
P25 ; P75		-16.7 ; 8.3
Mean (SD)		-4.9 (25.3)
Min ; Max		-100 ; 41.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

40 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Treatment - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	54
Median	18.8	37.5
P25 ; P75	9.4 ; 28.1	25.0 ; 59.4
Mean (SD)	18.8 (13.3)	41.7 (22.6)
Min ; Max	9.4 ; 28.1	9.4 ; 100.0
Week 24		
N		39
Median		25.0
P25 ; P75		6.3 ; 37.5
Mean (SD)		24.0 (19.2)
Min ; Max		0.0 ; 68.8
Week 32		
N		34
Median		25.0
P25 ; P75		6.3 ; 40.6
Mean (SD)		25.9 (20.3)
Min ; Max		0.0 ; 78.1
Change from baseline to week 24		
N		38
Median		-12.5
P25 ; P75		-31.3 ; -3.1
Mean (SD)		-16.9 (25.7)
Min ; Max		-87.5 ; 56.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

41 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Future - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	54
Median	55.0	50.0
P25 ; P75	45.0 ; 65.0	35.0 ; 65.0
Mean (SD)	55.0 (14.1)	48.1 (22.6)
Min ; Max	45.0 ; 65.0	0.0 ; 95.0
Week 24		
N		40
Median		32.5
P25 ; P75		20.0 ; 55.0
Mean (SD)		38.3 (23.5)
Min ; Max		5.0 ; 85.0
Week 32		
N		35
Median		35.0
P25 ; P75		20.0 ; 55.0
Mean (SD)		38.6 (24.0)
Min ; Max		5.0 ; 90.0
Change from baseline to week 24		
N		38
Median		-7.5
P25 ; P75		-25.0 ; 5.0
Mean (SD)		-11.3 (25.2)
Min ; Max		-70.0 ; 55.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

42 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Family planning - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	38
Median	30.2	25.0
P25 ; P75	18.8 ; 41.7	0.0 ; 43.8
Mean (SD)	30.2 (16.2)	25.9 (25.3)
Min ; Max	18.8 ; 41.7	0.0 ; 75.0
Week 24		
N		23
Median		0.0
P25 ; P75		0.0 ; 33.3
Mean (SD)		16.2 (26.0)
Min ; Max		0.0 ; 100.0
Week 32		
N		20
Median		0.0
P25 ; P75		0.0 ; 18.8
Mean (SD)		12.2 (19.1)
Min ; Max		0.0 ; 62.5
Change from baseline to week 24		
N		20
Median		0.0
P25 ; P75		-29.2 ; 3.1
Mean (SD)		-10.1 (22.4)
Min ; Max		-50.0 ; 31.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

43 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Partnership and sexuality - >= 17 years - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	3	80
N in FAS and ADS	2	68
Baseline		
N	2	54
Median	12.5	20.8
P25 ; P75	8.3 ; 16.7	0.0 ; 33.3
Mean (SD)	12.5 (5.9)	24.7 (25.5)
Min ; Max	8.3 ; 16.7	0.0 ; 100.0
Week 24		
N		40
Median		8.3
P25 ; P75		0.0 ; 25.0
Mean (SD)		19.0 (28.1)
Min ; Max		0.0 ; 100.0
Week 32		
N		36
Median		16.7
P25 ; P75		0.0 ; 41.7
Mean (SD)		24.1 (29.5)
Min ; Max		0.0 ; 100.0
Change from baseline to week 24		
N		39
Median		0.0
P25 ; P75		-25.0 ; 8.3
Mean (SD)		-5.3 (28.8)
Min ; Max		-83.3 ; 50.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

44 Haemophilia treament experience measure (Hemo-TEM) - Total score - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	11.7	22.0
P25 ; P75	9.3 ; 27.0	10.7 ; 37.1
Mean (SD)	16.0 (9.6)	26.4 (20.6)
Min ; Max	9.3 ; 27.0	0.0 ; 85.5
Week 24		
N	5	83
Median	3.3	5.7
P25 ; P75	2.5 ; 4.2	2.3 ; 13.6
Mean (SD)	3.3 (2.5)	9.3 (10.1)
Min ; Max	0.0 ; 6.7	0.0 ; 44.3
Week 32		
N	5	80
Median	1.7	6.3
P25 ; P75	1.5 ; 2.5	2.5 ; 13.1
Mean (SD)	2.7 (3.1)	8.9 (8.5)
Min ; Max	0.0 ; 8.0	0.0 ; 40.8
Change from baseline to week 24		
N	3	58
Median	-11.7	-9.8
P25 ; P75	-20.3 ; -5.2	-27.7 ; 0.0
Mean (SD)	-12.4 (7.6)	-17.0 (22.7)
Min ; Max	-20.3 ; -5.2	-81.3 ; 13.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

45 Haemophilia treament experience measure (Hemo-TEM) - Injection difficulties - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	16.7	16.7
P25 ; P75	0.0 ; 41.7	0.0 ; 41.7
Mean (SD)	19.4 (21.0)	25.7 (27.6)
Min ; Max	0.0 ; 41.7	0.0 ; 100.0
Week 24		
N	5	83
Median	8.3	0.0
P25 ; P75	0.0 ; 8.3	0.0 ; 16.7
Mean (SD)	5.0 (4.6)	8.3 (12.9)
Min ; Max	0.0 ; 8.3	0.0 ; 75.0
Week 32		
N	5	80
Median	0.0	0.0
P25 ; P75	0.0 ; 8.3	0.0 ; 8.3
Mean (SD)	6.7 (10.9)	7.3 (13.9)
Min ; Max	0.0 ; 25.0	0.0 ; 75.0
Change from baseline to week 24		
N	3	58
Median	-16.7	-8.3
P25 ; P75	-41.7 ; 8.3	-33.3 ; 0.0
Mean (SD)	-16.7 (25.0)	-17.5 (30.7)
Min ; Max	-41.7 ; 8.3	-100 ; 50.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

46 Haemophilia treament experience measure (Hemo-TEM) - Physical impact - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	33.3	25.0
P25 ; P75	4.2 ; 33.3	12.5 ; 41.7
Mean (SD)	23.6 (16.8)	27.2 (18.9)
Min ; Max	4.2 ; 33.3	0.0 ; 79.2
Week 24		
N	5	83
Median	4.2	8.3
P25 ; P75	0.0 ; 8.3	0.0 ; 16.7
Mean (SD)	5.0 (5.4)	12.4 (13.5)
Min ; Max	0.0 ; 12.5	0.0 ; 54.2
Week 32		
N	5	80
Median	4.2	10.4
P25 ; P75	4.2 ; 4.2	4.2 ; 20.8
Mean (SD)	4.2 (2.9)	14.1 (13.2)
Min ; Max	0.0 ; 8.3	0.0 ; 58.3
Change from baseline to week 24		
N	3	58
Median	-20.8	-6.3
P25 ; P75	-33.3 ; -4.2	-20.8 ; 0.0
Mean (SD)	-19.4 (14.6)	-13.9 (21.3)
Min ; Max	-33.3 ; -4.2	-66.7 ; 12.5

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

47 Haemophilia treament experience measure (Hemo-TEM) - Interference - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	6.3	25.0
P25 ; P75	0.0 ; 25.0	6.3 ; 50.0
Mean (SD)	10.4 (13.0)	30.5 (28.8)
Min ; Max	0.0 ; 25.0	0.0 ; 100.0
Week 24		
N	5	83
Median	0.0	0.0
P25 ; P75	0.0 ; 6.3	0.0 ; 12.5
Mean (SD)	3.8 (5.6)	6.6 (10.2)
Min ; Max	0.0 ; 12.5	0.0 ; 41.7
Week 32		
N	5	80
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 7.3
Mean (SD)	0.0 (0.0)	5.8 (9.4)
Min ; Max	0.0 ; 0.0	0.0 ; 37.5
Change from baseline to week 24		
N	3	58
Median	0.0	-17.7
P25 ; P75	-18.8 ; 6.3	-41.7 ; 0.0
Mean (SD)	-4.2 (13.0)	-24.4 (31.6)
Min ; Max	-18.8 ; 6.3	-100 ; 18.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

48 Haemophilia treament experience measure (Hemo-TEM) - Treatment bother - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	7.1	14.3
P25 ; P75	0.0 ; 39.3	3.6 ; 35.7
Mean (SD)	15.5 (20.9)	23.6 (24.4)
Min ; Max	0.0 ; 39.3	0.0 ; 92.9
Week 24		
N	5	83
Median	0.0	3.6
P25 ; P75	0.0 ; 0.0	0.0 ; 10.7
Mean (SD)	2.1 (4.8)	7.9 (13.3)
Min ; Max	0.0 ; 10.7	0.0 ; 85.7
Week 32		
N	5	80
Median	0.0	3.6
P25 ; P75	0.0 ; 3.6	0.0 ; 10.7
Mean (SD)	2.9 (4.7)	6.3 (8.6)
Min ; Max	0.0 ; 10.7	0.0 ; 39.3
Change from baseline to week 24		
N	3	58
Median	-7.1	-8.9
P25 ; P75	-28.6 ; 0.0	-28.6 ; 0.0
Mean (SD)	-11.9 (14.9)	-15.8 (29.2)
Min ; Max	-28.6 ; 0.0	-92.9 ; 85.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

49 Haemophilia treament experience measure (Hemo-TEM) - Emotional impact - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Baseline		
N	3	63
Median	12.5	20.8
P25 ; P75	0.0 ; 20.8	4.2 ; 41.7
Mean (SD)	11.1 (10.5)	25.0 (23.8)
Min ; Max	0.0 ; 20.8	0.0 ; 100.0
Week 24		
N	5	83
Median	0.0	4.2
P25 ; P75	0.0 ; 0.0	0.0 ; 16.7
Mean (SD)	0.8 (1.9)	11.0 (15.2)
Min ; Max	0.0 ; 4.2	0.0 ; 55.0
Week 32		
N	5	80
Median	0.0	4.2
P25 ; P75	0.0 ; 0.0	0.0 ; 20.8
Mean (SD)	0.0 (0.0)	11.1 (12.9)
Min ; Max	0.0 ; 0.0	0.0 ; 50.0
Change from baseline to week 24		
N	3	58
Median	-12.5	-4.2
P25 ; P75	-16.7 ; 0.0	-20.8 ; 0.0
Mean (SD)	-9.7 (8.7)	-13.4 (25.2)
Min ; Max	-16.7 ; 0.0	-100 ; 25.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

50 Haemophilia patient preference questionnaire (H-PPQ) - US vs non-US - week 24 - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non US
N in FAS	6	108
N in FAS and ADS	5	94
1. Overall, which treatment do you prefer?		
Current treatment	4 (80.0)	73 (77.7)
Previous treatment	0	1 (1.1)
No preference	1 (20.0)	4 (4.3)
Missing	0	16 (17.0)
For subjects preferring current treatment:		
N preferring current treatment	4 (100)	73 (100)
2. How strong is this treatment preference (indicated in question 1)?		
Very strong	3 (75.0)	49 (67.1)
Fairly strong	1 (25.0)	21 (28.8)
Not very strong	0	3 (4.1)
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	2 (50.0)	15 (20.5)
Feels less emotionally distressing	0	12 (16.4)
Less painful to inject	2 (50.0)	23 (31.5)
How often do you have to inject	0	6 (8.2)
Fewer bleeds	3 (75.0)	55 (75.3)
Require less time	1 (25.0)	32 (43.8)
Other reason	0	3 (4.1)
For subjects preferring previous treatment:		
N preferring previous treatment	0	1 (100)
2. How strong is this treatment preference (indicated in question 1)?		

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

Haemophilia patient preference questionnaire (H-PPQ) - US vs non-US - week 24 - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non US
Very strong	0	1 (100)
Fairly strong	0	0
Not very strong	0	0
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	0	0
Feels less emotionally distressing	0	1 (100)
Less painful to inject	0	1 (100)
How often do you have to inject	0	0
Fewer bleeds	0	0
Require less time	0	0
Other reason	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

51 Patient global impression of severity (PGI-S) - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Level of physical functioning over the past week		
Baseline		
N	3 (100)	59 (100)
Very good		5 (8.5)
Good	2 (66.7)	19 (32.2)
Fair		20 (33.9)
Poor	1 (33.3)	6 (10.2)
Very poor		9 (15.3)
Week 4		
N	3 (100)	60 (100)
Very good	1 (33.3)	14 (23.3)
Good		26 (43.3)
Fair	2 (66.7)	16 (26.7)
Poor		4 (6.7)
Week 8		
N	4 (100)	75 (100)
Very good	1 (25.0)	21 (28.0)
Good	2 (50.0)	29 (38.7)
Fair	1 (25.0)	19 (25.3)
Poor		5 (6.7)
Very poor		1 (1.3)
Week 16		
N	4 (100)	70 (100)
Very good	1 (25.0)	21 (30.0)
Good	2 (50.0)	28 (40.0)
Fair	1 (25.0)	16 (22.9)
Poor		5 (7.1)
Week 24		
N	5 (100)	78 (100)
Very good	1 (20.0)	21 (26.9)
Good	3 (60.0)	31 (39.7)
Fair	1 (20.0)	21 (26.9)
Poor		5 (6.4)
Week 32		
N	5 (100)	75 (100)
Very good	2 (40.0)	23 (30.7)
Good	1 (20.0)	25 (33.3)
Fair	2 (40.0)	22 (29.3)
Poor		3 (4.0)
Very poor		2 (2.7)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

52 Patient global impression of change (PGI-C) - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
N in FAS	6	108
N in FAS and ADS	5	94
Overall change in your level of physical functioning since you started taking the study medication		
Week 4		
N	3 (100)	59 (100)
Very much better	1 (33.3)	23 (39.0)
Moderately better		24 (40.7)
A little better	1 (33.3)	9 (15.3)
No change	1 (33.3)	3 (5.1)
Week 8		
N	4 (100)	74 (100)
Very much better	2 (50.0)	37 (50.0)
Moderately better	1 (25.0)	20 (27.0)
A little better		11 (14.9)
No change	1 (25.0)	5 (6.8)
Moderately worse		1 (1.4)
Week 16		
N	4 (100)	69 (100)
Very much better	2 (50.0)	37 (53.6)
Moderately better	2 (50.0)	22 (31.9)
A little better		8 (11.6)
No change		2 (2.9)
Week 24		
N	5 (100)	78 (100)
Very much better	3 (60.0)	43 (55.1)
Moderately better	1 (20.0)	23 (29.5)
A little better		8 (10.3)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

Patient global impression of change (PGI-C) - US vs non-US - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	US	non-US
No change	1 (20.0)	4 (5.1)
Week 32		
N	5 (100)	75 (100)
Very much better	4 (80.0)	43 (57.3)
Moderately better		22 (29.3)
A little better		6 (8.0)
No change	1 (20.0)	2 (2.7)
A little worse		2 (2.7)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

53 Bleeding episodes - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX				
	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
N in FAS	1	1	1	4	6	6
N in FAS and ADS	1	1	1	4	6	6
Person years of exposure in ADS	0.3	1.1	1.2	3.1	5.4	5.4
Weeks of exposure in ADS						
Median	16.3	55.9	64.1	39.8	56.1	56.1
P25 ; P75	16.3 ; 16.3	55.9 ; 55.9	64.1 ; 64.1	20.3 ; 60.3	23.1 ; 64.1	23.1 ; 64.1
Mean (SD)				40.3 (23.4)	46.9 (21.0)	46.9 (21.0)
Min ; Max	16.3 ; 16.3	55.9 ; 55.9	64.1 ; 64.1	17.4 ; 64.1	17.4 ; 64.1	17.4 ; 64.1
Treated spontaneous and traumatic bleeding episodes						
Number of episodes	1	18	2	11	31	31
ABR						
Median	3.2	16.8	1.6	3.0	3.0	3.0
P25 ; P75	3.2 ; 3.2	16.8 ; 16.8	1.6 ; 1.6	1.4 ; 7.6	1.6 ; 12.0	1.6 ; 12.0
Mean (SD)				4.5 (5.2)	6.1 (6.7)	6.1 (6.7)
Min ; Max	3.2 ; 3.2	16.8 ; 16.8	1.6 ; 1.6	0.0 ; 12.0	0.0 ; 16.8	0.0 ; 16.8
Treated spontaneous bleeding episodes						
Number of episodes	1	18	2	6	26	26
ABR						
Median	3.2	16.8	1.6	1.2	2.0	2.0
P25 ; P75	3.2 ; 3.2	16.8 ; 16.8	1.6 ; 1.6	0.0 ; 5.7	0.0 ; 9.0	0.0 ; 9.0
Mean (SD)				2.9 (4.2)	5.0 (6.7)	5.0 (6.7)
Min ; Max	3.2 ; 3.2	16.8 ; 16.8	1.6 ; 1.6	0.0 ; 9.0	0.0 ; 16.8	0.0 ; 16.8
Treated spontaneous and traumatic joint bleeding episodes						

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation,
Min: minimum, Max: maximum, ABR: annualised bleeding rate
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX				
	Arm 1	Arm 2	Arm 3	Arm 4	Arms 2-4	Total
Number of episodes	1	11	1	7	19	19
ABR						
Median	3.2	10.3	0.8	1.4	1.8	1.8
P25 ; P75	3.2 ; 3.2	10.3 ; 10.3	0.8 ; 0.8	0.0 ; 3.0	0.0 ; 3.3	0.0 ; 3.3
Mean (SD)				1.5 (1.8)	2.9 (3.9)	2.9 (3.9)
Min ; Max	3.2 ; 3.2	10.3 ; 10.3	0.8 ; 0.8	0.0 ; 3.3	0.0 ; 10.3	0.0 ; 10.3
Treated spontaneous and traumatic target joint bleeding episodes						
Number of episodes	0	4	0	4	8	8
ABR						
Median	0.0	3.7	0.0	0.0	0.0	0.0
P25 ; P75	0.0 ; 0.0	3.7 ; 3.7	0.0 ; 0.0	0.0 ; 1.6	0.0 ; 3.3	0.0 ; 3.3
Mean (SD)				0.8 (1.6)	1.2 (1.8)	1.2 (1.8)
Min ; Max	0.0 ; 0.0	3.7 ; 3.7	0.0 ; 0.0	0.0 ; 3.3	0.0 ; 3.7	0.0 ; 3.7
All treated and untreated spontaneous and traumatic bleeding episodes						
Number of episodes	1	19	7	19	45	45
ABR						
Median	3.2	17.7	5.7	6.3	7.5	7.5
P25 ; P75	3.2 ; 3.2	17.7 ; 17.7	5.7 ; 5.7	2.8 ; 10.6	3.3 ; 12.0	3.3 ; 12.0
Mean (SD)				6.7 (4.7)	8.4 (5.9)	8.4 (5.9)
Min ; Max	3.2 ; 3.2	17.7 ; 17.7	5.7 ; 5.7	2.3 ; 12.0	2.3 ; 17.7	2.3 ; 17.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, P25/P75 is the 25th/75th percentile, SD: standard deviation,
Min: minimum, Max: maximum, ABR: annualised bleeding rate
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

54 Bleeding episodes - by haemophilia type - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Haemophilia A	Haemophilia B
N in FAS	1	5
N in FAS and ADS	1	5
Person years of exposure in ADS	0.4	4.9
Weeks of exposure in ADS		
Median	23.1	56.4
P25 ; P75	23.1 ; 23.1	55.9 ; 64.1
Mean (SD)		51.6 (19.5)
Min ; Max	23.1 ; 23.1	17.4 ; 64.1
Primary endpoint:		
Treated spontaneous and traumatic bleeding episodes		
Number of episodes	0	31
ABR		
Median	0.0	3.3
P25 ; P75	0.0 ; 0.0	2.8 ; 12.0
Mean (SD)		7.3 (6.7)
Min ; Max	0.0 ; 0.0	1.6 ; 16.8
Treated spontaneous bleeding episodes		
Number of episodes	0	26
ABR		
Median	0.0	2.4
P25 ; P75	0.0 ; 0.0	1.6 ; 9.0
Mean (SD)		6.0 (7.0)
Min ; Max	0.0 ; 0.0	0.0 ; 16.8
Treated spontaneous and traumatic joint bleeding episodes		
Number of episodes	0	19
ABR		
Median	0.0	2.8
P25 ; P75	0.0 ; 0.0	0.8 ; 3.3
Mean (SD)		3.4 (4.1)
Min ; Max	0.0 ; 0.0	0.0 ; 10.3
Treated spontaneous and traumatic target joint bleeding episodes		
Number of episodes	0	8
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 3.3
Mean (SD)		1.4 (1.9)
Min ; Max	0.0 ; 0.0	0.0 ; 3.7
All treated and untreated spontaneous and traumatic bleeding episodes		
Number of episodes	1	44
ABR		
Median	2.3	9.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - by haemophilia type - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Haemophilia A	Haemophilia B
P25 ; P75	2.3 ; 2.3	5.7 ; 12.0
Mean (SD)		9.6 (5.7)
Min ; Max	2.3 ; 2.3	3.3 ; 17.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

55 Bleeding episodes - by age group - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
N in FAS	1	5
N in FAS and ADS	1	5
Person years of exposure in ADS	1.1	4.3
Weeks of exposure in ADS		
Median	56.4	55.9
P25 ; P75	56.4 ; 56.4	23.1 ; 64.1
Mean (SD)		44.9 (22.9)
Min ; Max	56.4 ; 56.4	17.4 ; 64.1
Primary endpoint:		
Treated spontaneous and traumatic bleeding episodes		
Number of episodes	3	28
ABR		
Median	2.8	3.3
P25 ; P75	2.8 ; 2.8	1.6 ; 12.0
Mean (SD)		6.7 (7.3)
Min ; Max	2.8 ; 2.8	0.0 ; 16.8
Treated spontaneous bleeding episodes		
Number of episodes	0	26
ABR		
Median	0.0	2.4
P25 ; P75	0.0 ; 0.0	1.6 ; 9.0
Mean (SD)		6.0 (7.0)
Min ; Max	0.0 ; 0.0	0.0 ; 16.8
Treated spontaneous and traumatic joint bleeding episodes		
Number of episodes	3	16
ABR		
Median	2.8	0.8
P25 ; P75	2.8 ; 2.8	0.0 ; 3.3
Mean (SD)		2.9 (4.4)
Min ; Max	2.8 ; 2.8	0.0 ; 10.3
Treated spontaneous and traumatic target joint bleeding episodes		
Number of episodes	0	8
ABR		
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 3.3
Mean (SD)		1.4 (1.9)
Min ; Max	0.0 ; 0.0	0.0 ; 3.7
All treated and untreated spontaneous and traumatic bleeding episodes		
Number of episodes	10	35
ABR		
Median	9.2	5.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

Bleeding episodes - by age group - Japanese subjects - descriptive statistics - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

	Concizumab PPX (arms 1-4)	
	Adolescents	Adults
P25 ; P75	9.2 ; 9.2	3.3 ; 12.0
Mean (SD)		8.2 (6.5)
Min ; Max	9.2 ; 9.2	2.3 ; 17.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens, PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum, ABR: annualised bleeding rate.
P25/P75 is the 25th/75th percentile.
All endpoints other than 'Treated spontaneous bleeding episodes' includes bleeding episodes with missing cause.

56 Subject disposition - Japanese subjects - summary - HAwI+HBwI - all subjects - trial 4311

	Previous OnD treatment		Concizumab Non-naive	Concizumab Naive	
	No PPX (arm 1) N (%)	Concizumab PPX (arm 2) N (%)	Concizumab PPX (arm 3) N (%)	Concizumab PPX (arm 4) N (%)	Total N (%)
Screened					7
Screening failures					0
Withdrawn before initial randomisation/allocation					0
Randomised/allocated	1 (100.0)	1 (100.0)	1 (100.0)	4 (100.0)	7 (100.0)
Exposed		1 (100.0)	1 (100.0)	4 (100.0)	6 (100.0)
Completed treatment at PACO [a]	0	1 (100.0)	1 (100.0)	2 (50.0)	4 (57.1)
Discontinued treatment		0	0	2 (50.0)	2 (33.3)
Adverse Event		0	0	0	0
Protocol deviation		0	0	0	0
Lack of efficacy		0	0	0	0
Lost to follow-up		0	0	0	0
Technical problems		0	0	0	0
Discretion of Investigator		0	0	0	0
Other		0	0	2 (50.0)	2 (33.3)
Withdrawn from trial	1 (100.0)	0	0	2 (50.0)	3 (42.9)
Withdrawal of consent [b]	1 (100.0)	0	0	2 (50.0)	3 (42.9)
Lost to follow-up	0	0	0	0	0
Investigator decision	0	0	0	0	0
Death	0	0	0	0	0
Full analysis set	1 (100.0)	1 (100.0)	1 (100.0)	4 (100.0)	7 (100.0)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors.
PPX: Prophylaxis, N: number of subjects, %: Percentage of randomised/allocated subjects, OnD: on-demand, PACO: Primary analyses cut-off.
[a]: Randomised/allocated subjects who did not discontinue treatment prior to week 24/32 (depending on arm).
[b]: withdrawal of consent by subject, subject's parent or subject's legally acceptable representative (LAR).
Subjects in arm 4 were previously on prophylaxis with by-passing agents or treated on-demand.

57 Subject disposition up until restart - Japanese subjects - summary - HAwI+HBwI - all subjects - trial 4311

	Previous OnD treatment		Concizumab Non-naive	Concizumab Naive	
	No PPX (arm 1) N (%)	Concizumab PPX (arm 2) N (%)	Concizumab PPX (arm 3) N (%)	Concizumab PPX (arm 4) N (%)	Total N (%)
Initial start - pause [a]					
Randomised/allocated	1	1	1	4	7
Exposed		1	1	4	6
Discontinued treatment		0	0	1	1
Adverse Event		0	0	0	0
Protocol deviation		0	0	0	0
Lack of efficacy		0	0	0	0
Lost to follow-up		0	0	0	0
Technical problems		0	0	0	0
Discretion of Investigator		0	0	0	0
Other		0	0	1	1
Withdrawn from trial	0	0	0	0	0
Withdrawal of consent [b]	0	0	0	0	0
Lost to follow-up	0	0	0	0	0
Investigator decision	0	0	0	0	0
Death	0	0	0	0	0
Pause [a] - restart [c]					
Subjects not re-consenting	1	0	0	1	2
Withdrawn from trial	1	0	0	1	2
Withdrawal of consent [b]	1	0	0	1	2
Lost to follow-up	0	0	0	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors.
N: number of subjects, OnD: on-demand. PPX: Prophylaxis, %: Percentage of randomised/allocated subjects.
[a]: NN put the project on pause 16-Mar-2020.
[b]: withdrawal of consent by subject, subject's parent or subject's legally acceptable representative (LAR).
[c]: Restart for a patient is defined as the reconsent date.
Subjects in arm 4 were previously on prophylaxis with by-passing agents or treated on-demand.

Subject disposition up until restart - Japanese subjects - summary - HAwI+HBwI - all subjects - trial 4311

	Previous OnD treatment		Concizumab Non-naive	Concizumab Naive	
	No PPX (arm 1) N (%)	Concizumab PPX (arm 2) N (%)	Concizumab PPX (arm 3) N (%)	Concizumab PPX (arm 4) N (%)	Total N (%)
Investigator decision	0	0	0	0	0
Death	0	0	0	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors.
N: number of subjects, OnD: on-demand. PPX: Prophylaxis, %: Percentage of randomised/allocated subjects.
[a]: NN put the project on pause 16-Mar-2020.
[b]: withdrawal of consent by subject, subject's parent or subject's legally acceptable representative (LAR).
[c]: Restart for a patient is defined as the reconsent date.
Subjects in arm 4 were previously on prophylaxis with by-passing agents or treated on-demand.

58 Subject disposition after restart - Japanese subjects - summary - HAwI+HBwI - all subjects - trial 4311

	Previous OnD treatm	Concizumab Non-naive	Concizumab Naive
	Concizumab PPX (arm 2) N	Concizumab PPX (arm 3) N	Concizumab PPX (arm 4) N
Subjects restarting [a]	1	1	3
Randomised/allocated [b]	0	0	0
Exposed	1	1	3
Discontinued treatment	0	0	1
Adverse Event	0	0	0
Protocol deviation	0	0	0
Lack of efficacy	0	0	0
Lost to follow-up	0	0	0
Technical problems	0	0	0
Discretion of Investigator	0	0	0
Other	0	0	1
Withdrawn from trial	0	0	1
Withdrawal of consent [c]	0	0	1
Lost to follow-up	0	0	0
Investigator decision	0	0	0
Death	0	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors.
N: number of subjects, OnD: on-demand, PPX: Prophylaxis
[a]: Restarting is defined as having a reconsent date.
[b]: Subjects who enters the trial after the restart.
[c]: Withdrawal of consent by subject, subject’s parent or subject’s legally acceptable representative (LAR).
Subjects in arm 4 were previously on prophylaxis with by-passing agents or treated on-demand.

59 Concizumab maintenance dose level - Japanese subjects - summary - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX			Total
	(Arm 2) N (%)	(Arm 3) N (%)	(Arm 4) N (%)	N (%)
Number of subjects	1	1	3	5
Maintenance dose level				
N	1	1	3	5
0.25 mg/kg	1 (100.0)	0	0	1 (20.0)
0.20 mg/kg	0	1 (100.0)	3 (100.0)	4 (80.0)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen.
PPX: Prophylaxis, %: Percentage of randomised/allocated subjects, N: number of subjects, %: percentage of subjects.

60 SF-36v2 (standard version) - bodily pain - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	42.2	42.6
P25 ; P75	38.2 ; 51.5	34.2 ; 47.5
Mean (SD)	43.6 (9.9)	41.7 (10.3)
Min ; Max	21.7 ; 62.0	21.7 ; 62.0
Week 24		
N	58	32
Median	53.5	50.7
P25 ; P75	46.7 ; 62.0	42.2 ; 54.7
Mean (SD)	52.4 (9.6)	48.7 (8.7)
Min ; Max	30.6 ; 62.0	34.6 ; 62.0
Week 32		
N	57	31
Median	51.5	50.7
P25 ; P75	46.7 ; 62.0	38.6 ; 62.0
Mean (SD)	50.6 (10.3)	49.6 (10.4)
Min ; Max	25.7 ; 62.0	30.6 ; 62.0
Change from baseline to week 24		
N	41	25
Median	4.8	6.5
P25 ; P75	0.0 ; 12.5	0.0 ; 10.5
Mean (SD)	6.9 (9.7)	7.0 (10.1)
Min ; Max	-13.3 ; 27.8	-13.3 ; 29.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

61 SF-36v2 (standard version) - bodily pain - by age - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	44.5	42.2
P25 ; P75	38.2 ; 55.6	34.6 ; 46.7
Mean (SD)	45.2 (11.8)	41.5 (8.7)
Min ; Max	21.7 ; 62.0	21.7 ; 62.0
Week 24		
N	30	60
Median	62.0	46.7
P25 ; P75	50.7 ; 62.0	42.2 ; 55.6
Mean (SD)	56.1 (7.7)	48.6 (9.2)
Min ; Max	38.2 ; 62.0	30.6 ; 62.0
Week 32		
N	32	56
Median	62.0	46.7
P25 ; P75	51.1 ; 62.0	38.2 ; 55.6
Mean (SD)	54.9 (9.2)	47.6 (10.0)
Min ; Max	34.2 ; 62.0	25.7 ; 62.0
Change from baseline to week 24		
N	24	42
Median	9.9	4.0
P25 ; P75	0.0 ; 16.3	0.0 ; 9.3
Mean (SD)	10.0 (9.8)	5.2 (9.4)
Min ; Max	-4.8 ; 29.8	-13.3 ; 29.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

62 SF-36v2 (standard version) - physical functioning - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	42.2	34.6
P25 ; P75	32.7 ; 48.9	26.9 ; 48.0
Mean (SD)	40.7 (9.9)	36.6 (12.3)
Min ; Max	21.2 ; 57.5	19.3 ; 57.5
Week 24		
N	58	32
Median	49.9	45.1
P25 ; P75	38.4 ; 53.7	33.6 ; 52.8
Mean (SD)	46.2 (10.1)	42.6 (11.5)
Min ; Max	21.2 ; 57.5	21.2 ; 57.5
Week 32		
N	57	31
Median	49.9	44.2
P25 ; P75	36.5 ; 53.7	32.7 ; 51.8
Mean (SD)	45.8 (10.2)	41.8 (12.1)
Min ; Max	25.0 ; 57.5	19.3 ; 57.5
Change from baseline to week 24		
N	41	25
Median	3.8	3.8
P25 ; P75	0.0 ; 7.7	0.0 ; 7.7
Mean (SD)	3.4 (6.3)	5.4 (7.8)
Min ; Max	-15.3 ; 17.2	-3.8 ; 30.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

63 SF-36v2 (standard version) - physical functioning - by age - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	45.1	40.3
P25 ; P75	30.8 ; 49.9	30.8 ; 44.2
Mean (SD)	41.6 (11.7)	37.7 (10.4)
Min ; Max	21.2 ; 57.5	19.3 ; 57.5
Week 24		
N	30	60
Median	53.7	44.2
P25 ; P75	42.2 ; 55.6	37.4 ; 51.8
Mean (SD)	48.2 (11.1)	43.3 (10.2)
Min ; Max	21.2 ; 57.5	21.2 ; 57.5
Week 32		
N	32	56
Median	53.7	44.2
P25 ; P75	38.4 ; 57.5	34.6 ; 49.9
Mean (SD)	48.6 (10.9)	42.0 (10.4)
Min ; Max	21.2 ; 57.5	19.3 ; 57.5
Change from baseline to week 24		
N	24	42
Median	3.8	3.8
P25 ; P75	0.0 ; 7.7	-1.9 ; 7.7
Mean (SD)	3.4 (6.0)	4.5 (7.5)
Min ; Max	-15.3 ; 13.4	-5.8 ; 30.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

64 SF-36v2 (standard version) - Role - Physical - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	41.4	39.2
P25 ; P75	37.0 ; 48.2	34.7 ; 45.9
Mean (SD)	41.8 (8.6)	39.2 (10.9)
Min ; Max	21.2 ; 57.2	21.2 ; 57.2
Week 24		
N	58	32
Median	48.2	48.2
P25 ; P75	41.4 ; 54.9	40.3 ; 53.8
Mean (SD)	47.8 (8.1)	47.3 (7.6)
Min ; Max	21.2 ; 57.2	30.2 ; 57.2
Week 32		
N	57	31
Median	48.2	48.2
P25 ; P75	41.4 ; 57.2	41.4 ; 54.9
Mean (SD)	47.3 (9.1)	46.4 (9.4)
Min ; Max	25.7 ; 57.2	21.2 ; 57.2
Change from baseline to week 24		
N	41	25
Median	4.5	4.5
P25 ; P75	0.0 ; 13.5	2.3 ; 11.2
Mean (SD)	4.7 (9.8)	6.8 (8.7)
Min ; Max	-18.0 ; 22.5	-9.0 ; 26.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

65 SF-36v2 (standard version) - Role - Physical - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	41.4	39.2
P25 ; P75	39.2 ; 50.4	34.7 ; 45.9
Mean (SD)	42.6 (9.8)	39.7 (9.3)
Min ; Max	21.2 ; 57.2	21.2 ; 57.2
Week 24		
N	30	60
Median	51.5	48.2
P25 ; P75	45.9 ; 57.2	39.2 ; 52.7
Mean (SD)	49.8 (7.9)	46.5 (7.7)
Min ; Max	30.2 ; 57.2	21.2 ; 57.2
Week 32		
N	32	56
Median	54.9	45.9
P25 ; P75	45.9 ; 57.2	40.3 ; 52.7
Mean (SD)	49.8 (8.8)	45.4 (9.1)
Min ; Max	25.7 ; 57.2	21.2 ; 57.2
Change from baseline to week 24		
N	24	42
Median	4.5	4.5
P25 ; P75	0.0 ; 13.5	0.0 ; 11.2
Mean (SD)	5.9 (8.1)	5.3 (10.1)
Min ; Max	-9.0 ; 18.0	-18.0 ; 26.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

66 SF-36v2 (standard version) - General Health - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	44.4	43.7
P25 ; P75	36.1 ; 48.4	35.6 ; 53.2
Mean (SD)	41.9 (9.8)	42.4 (11.3)
Min ; Max	21.3 ; 66.5	21.3 ; 61.7
Week 24		
N	58	32
Median	48.4	48.4
P25 ; P75	41.3 ; 54.6	43.7 ; 58.7
Mean (SD)	48.3 (9.4)	49.6 (9.7)
Min ; Max	28.5 ; 66.5	26.1 ; 66.5
Week 32		
N	57	31
Median	50.8	50.8
P25 ; P75	43.7 ; 57.0	38.9 ; 57.0
Mean (SD)	49.5 (10.4)	47.8 (10.4)
Min ; Max	26.1 ; 66.5	28.5 ; 66.5
Change from baseline to week 24		
N	41	25
Median	3.8	4.8
P25 ; P75	0.0 ; 10.5	0.0 ; 12.8
Mean (SD)	5.5 (9.6)	6.2 (11.7)
Min ; Max	-12.8 ; 31.9	-13.3 ; 34.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

67 SF-36v2 (standard version) - General Health - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	45.6	43.7
P25 ; P75	38.9 ; 53.2	34.2 ; 46.1
Mean (SD)	44.8 (10.3)	40.5 (10.1)
Min ; Max	21.3 ; 66.5	21.3 ; 61.7
Week 24		
N	30	60
Median	53.2	46.1
P25 ; P75	48.4 ; 59.4	39.6 ; 52.0
Mean (SD)	53.3 (7.3)	46.5 (9.7)
Min ; Max	33.2 ; 66.5	26.1 ; 66.5
Week 32		
N	32	56
Median	53.9	43.7
P25 ; P75	51.5 ; 58.7	37.3 ; 55.6
Mean (SD)	54.5 (8.0)	45.6 (10.2)
Min ; Max	33.2 ; 66.5	26.1 ; 64.1
Change from baseline to week 24		
N	24	42
Median	6.2	2.4
P25 ; P75	0.0 ; 12.8	-2.4 ; 10.5
Mean (SD)	8.5 (9.5)	4.2 (10.6)
Min ; Max	-4.8 ; 31.9	-13.3 ; 34.2

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

68 SF-36v2 (standard version) - Vitality - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	49.6	46.7
P25 ; P75	42.2 ; 55.6	40.7 ; 52.6
Mean (SD)	48.6 (9.8)	46.2 (9.3)
Min ; Max	28.8 ; 70.4	22.9 ; 61.5
Week 24		
N	58	32
Median	55.6	52.6
P25 ; P75	49.6 ; 61.5	49.6 ; 58.5
Mean (SD)	54.9 (7.8)	53.4 (7.5)
Min ; Max	37.7 ; 70.4	37.7 ; 64.5
Week 32		
N	57	31
Median	55.6	52.6
P25 ; P75	46.7 ; 61.5	46.7 ; 61.5
Mean (SD)	53.8 (9.0)	52.8 (10.1)
Min ; Max	34.8 ; 70.4	28.8 ; 70.4
Change from baseline to week 24		
N	41	25
Median	5.9	5.9
P25 ; P75	0.0 ; 11.9	0.0 ; 11.9
Mean (SD)	5.7 (9.0)	7.8 (12.1)
Min ; Max	-26.7 ; 20.8	-8.9 ; 41.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

69 SF-36v2 (standard version) - Vitality - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	49.6	46.7
P25 ; P75	43.7 ; 55.6	37.7 ; 52.6
Mean (SD)	50.5 (9.9)	46.1 (9.2)
Min ; Max	22.9 ; 70.4	28.8 ; 64.5
Week 24		
N	30	60
Median	57.1	52.6
P25 ; P75	52.6 ; 61.5	48.1 ; 61.5
Mean (SD)	56.4 (6.5)	53.4 (8.1)
Min ; Max	40.7 ; 70.4	37.7 ; 70.4
Week 32		
N	32	56
Median	58.5	49.6
P25 ; P75	52.6 ; 64.5	43.7 ; 58.5
Mean (SD)	57.8 (9.3)	51.0 (8.5)
Min ; Max	28.8 ; 70.4	31.8 ; 70.4
Change from baseline to week 24		
N	24	42
Median	5.9	5.9
P25 ; P75	-1.5 ; 10.4	0.0 ; 11.9
Mean (SD)	4.8 (12.2)	7.4 (8.9)
Min ; Max	-26.7 ; 41.6	-5.9 ; 32.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

70 SF-36v2 (standard version) - Social Functioning - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	42.3	42.3
P25 ; P75	37.3 ; 52.3	32.3 ; 47.3
Mean (SD)	43.0 (10.2)	41.7 (12.0)
Min ; Max	17.2 ; 57.3	17.2 ; 57.3
Week 24		
N	58	32
Median	49.8	52.3
P25 ; P75	42.3 ; 57.3	47.3 ; 57.3
Mean (SD)	49.3 (8.1)	50.0 (9.3)
Min ; Max	32.3 ; 57.3	17.2 ; 57.3
Week 32		
N	57	31
Median	47.3	52.3
P25 ; P75	37.3 ; 57.3	42.3 ; 57.3
Mean (SD)	47.6 (10.1)	49.1 (10.2)
Min ; Max	22.3 ; 57.3	17.2 ; 57.3
Change from baseline to week 24		
N	41	25
Median	5.0	5.0
P25 ; P75	0.0 ; 10.0	0.0 ; 10.0
Mean (SD)	4.9 (9.9)	7.8 (12.0)
Min ; Max	-15.0 ; 30.1	-10.0 ; 40.1

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

71 SF-36v2 (standard version) - Social Functioning - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	44.8	42.3
P25 ; P75	37.3 ; 52.3	32.3 ; 47.3
Mean (SD)	44.0 (11.3)	41.6 (10.6)
Min ; Max	17.2 ; 57.3	17.2 ; 57.3
Week 24		
N	30	60
Median	54.8	52.3
P25 ; P75	47.3 ; 57.3	42.3 ; 57.3
Mean (SD)	49.7 (10.0)	49.5 (7.7)
Min ; Max	17.2 ; 57.3	32.3 ; 57.3
Week 32		
N	32	56
Median	52.3	47.3
P25 ; P75	39.8 ; 57.3	42.3 ; 57.3
Mean (SD)	48.6 (11.1)	47.8 (9.6)
Min ; Max	17.2 ; 57.3	22.3 ; 57.3
Change from baseline to week 24		
N	24	42
Median	5.0	5.0
P25 ; P75	0.0 ; 10.0	0.0 ; 10.0
Mean (SD)	4.4 (11.6)	6.9 (10.3)
Min ; Max	-15.0 ; 40.1	-10.0 ; 30.1

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

72 SF-36v2 (standard version) - Role - Emotional - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	45.7	45.7
P25 ; P75	38.8 ; 56.2	31.8 ; 52.7
Mean (SD)	45.6 (10.1)	41.5 (12.0)
Min ; Max	21.4 ; 56.2	14.4 ; 56.2
Week 24		
N	58	32
Median	49.2	52.7
P25 ; P75	45.7 ; 56.2	40.5 ; 56.2
Mean (SD)	48.3 (8.9)	48.3 (8.8)
Min ; Max	14.4 ; 56.2	28.3 ; 56.2
Week 32		
N	57	31
Median	49.2	52.7
P25 ; P75	38.8 ; 56.2	38.8 ; 56.2
Mean (SD)	46.1 (10.7)	47.7 (9.3)
Min ; Max	21.4 ; 56.2	28.3 ; 56.2
Change from baseline to week 24		
N	41	25
Median	0.0	3.5
P25 ; P75	-3.5 ; 7.0	0.0 ; 10.5
Mean (SD)	3.2 (11.2)	5.7 (6.8)
Min ; Max	-31.3 ; 31.3	-3.5 ; 24.4

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

73 SF-36v2 (standard version) - Role - Emotional - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	45.7	45.7
P25 ; P75	35.3 ; 56.2	35.3 ; 56.2
Mean (SD)	44.0 (10.9)	44.1 (11.1)
Min ; Max	21.4 ; 56.2	14.4 ; 56.2
Week 24		
N	30	60
Median	52.7	45.7
P25 ; P75	45.7 ; 56.2	42.2 ; 56.2
Mean (SD)	49.9 (8.5)	47.5 (8.9)
Min ; Max	28.3 ; 56.2	14.4 ; 56.2
Week 32		
N	32	56
Median	54.4	45.7
P25 ; P75	44.0 ; 56.2	37.0 ; 56.2
Mean (SD)	49.1 (9.1)	45.3 (10.6)
Min ; Max	28.3 ; 56.2	21.4 ; 56.2
Change from baseline to week 24		
N	24	42
Median	1.7	0.0
P25 ; P75	0.0 ; 10.5	0.0 ; 10.4
Mean (SD)	4.8 (7.8)	3.8 (10.9)
Min ; Max	-7.0 ; 20.9	-31.3 ; 31.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

74 SF-36v2 (standard version) - Mental Health - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	46.9	48.3
P25 ; P75	37.8 ; 53.5	43.0 ; 53.5
Mean (SD)	45.8 (10.8)	46.9 (9.4)
Min ; Max	24.7 ; 64.0	19.5 ; 56.1
Week 24		
N	58	32
Median	52.2	53.5
P25 ; P75	45.6 ; 56.1	44.3 ; 57.4
Mean (SD)	49.8 (8.2)	51.2 (8.3)
Min ; Max	24.7 ; 64.0	35.2 ; 64.0
Week 32		
N	57	31
Median	50.9	50.9
P25 ; P75	43.0 ; 56.1	43.0 ; 56.1
Mean (SD)	49.3 (9.6)	49.7 (9.0)
Min ; Max	24.7 ; 64.0	27.3 ; 61.3
Change from baseline to week 24		
N	41	25
Median	2.6	2.6
P25 ; P75	-2.6 ; 10.5	-2.6 ; 10.5
Mean (SD)	4.0 (10.6)	4.5 (12.8)
Min ; Max	-13.1 ; 28.8	-15.7 ; 36.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

75 SF-36v2 (standard version) - Mental Health - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	50.9	48.3
P25 ; P75	40.4 ; 53.5	40.4 ; 53.5
Mean (SD)	47.5 (9.5)	45.4 (10.6)
Min ; Max	29.9 ; 64.0	19.5 ; 64.0
Week 24		
N	30	60
Median	53.5	49.6
P25 ; P75	45.6 ; 58.7	43.0 ; 56.1
Mean (SD)	52.4 (7.5)	49.3 (8.4)
Min ; Max	35.2 ; 64.0	24.7 ; 64.0
Week 32		
N	32	56
Median	53.5	50.9
P25 ; P75	46.9 ; 58.7	43.0 ; 53.5
Mean (SD)	51.5 (8.9)	48.3 (9.4)
Min ; Max	27.3 ; 64.0	24.7 ; 61.3
Change from baseline to week 24		
N	24	42
Median	6.5	1.3
P25 ; P75	-3.9 ; 10.5	-2.6 ; 7.9
Mean (SD)	4.4 (11.3)	4.0 (11.6)
Min ; Max	-15.7 ; 31.4	-13.1 ; 36.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

76 SF-36v2 (standard version) - Physical health component score - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	42.5	37.7
P25 ; P75	34.8 ; 46.7	30.3 ; 48.8
Mean (SD)	40.9 (8.3)	38.3 (10.5)
Min ; Max	19.8 ; 60.2	19.5 ; 55.6
Week 24		
N	58	32
Median	50.9	45.5
P25 ; P75	42.8 ; 55.0	39.9 ; 50.8
Mean (SD)	48.5 (9.7)	45.6 (8.6)
Min ; Max	25.1 ; 66.1	29.2 ; 60.4
Week 32		
N	57	31
Median	49.4	42.8
P25 ; P75	40.8 ; 56.8	37.2 ; 53.1
Mean (SD)	48.4 (10.2)	45.1 (10.6)
Min ; Max	23.2 ; 68.3	25.5 ; 70.6
Change from baseline to week 24		
N	41	25
Median	5.3	6.3
P25 ; P75	0.4 ; 10.3	1.7 ; 10.3
Mean (SD)	5.3 (6.8)	6.5 (8.6)
Min ; Max	-9.2 ; 18.1	-9.6 ; 28.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

77 SF-36v2 (standard version) - Physical health component score - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	44.9	38.2
P25 ; P75	36.9 ; 48.8	31.7 ; 43.6
Mean (SD)	42.8 (9.2)	38.2 (8.9)
Min ; Max	19.5 ; 60.2	19.8 ; 55.6
Week 24		
N	30	60
Median	54.6	45.6
P25 ; P75	45.8 ; 58.1	37.4 ; 51.9
Mean (SD)	51.6 (7.8)	45.4 (9.5)
Min ; Max	31.5 ; 62.3	25.1 ; 66.1
Week 32		
N	32	56
Median	54.3	45.2
P25 ; P75	43.6 ; 58.8	37.2 ; 50.5
Mean (SD)	52.1 (9.8)	44.5 (9.8)
Min ; Max	34.4 ; 70.6	23.2 ; 68.3
Change from baseline to week 24		
N	24	42
Median	7.5	5.4
P25 ; P75	2.8 ; 11.5	-0.3 ; 10.3
Mean (SD)	7.0 (6.3)	5.0 (8.1)
Min ; Max	-5.4 ; 20.2	-9.6 ; 28.6

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

78 SF-36v2 (standard version) - Mental health component score - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	44	27
Median	49.2	50.5
P25 ; P75	39.1 ; 55.3	39.6 ; 53.8
Mean (SD)	47.7 (10.4)	47.0 (9.3)
Min ; Max	25.7 ; 63.0	20.1 ; 57.6
Week 24		
N	58	32
Median	53.2	53.4
P25 ; P75	46.7 ; 57.0	46.4 ; 61.0
Mean (SD)	51.1 (8.9)	52.8 (9.3)
Min ; Max	29.7 ; 68.2	34.8 ; 68.4
Week 32		
N	57	31
Median	52.2	53.8
P25 ; P75	44.1 ; 57.2	46.0 ; 59.4
Mean (SD)	49.4 (10.5)	51.7 (10.5)
Min ; Max	20.8 ; 64.1	17.5 ; 69.5
Change from baseline to week 24		
N	41	25
Median	1.9	3.6
P25 ; P75	-2.4 ; 8.5	-0.4 ; 9.9
Mean (SD)	3.9 (10.4)	5.8 (11.5)
Min ; Max	-12.5 ; 34.0	-10.8 ; 37.9

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

79 SF-36v2 (standard version) - Mental health component score - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	26	45
Median	48.1	49.4
P25 ; P75	40.7 ; 56.5	39.0 ; 54.4
Mean (SD)	48.1 (8.7)	47.1 (10.6)
Min ; Max	30.5 ; 61.9	20.1 ; 63.0
Week 24		
N	30	60
Median	53.0	53.2
P25 ; P75	48.0 ; 57.0	46.0 ; 59.5
Mean (SD)	52.3 (8.3)	51.4 (9.4)
Min ; Max	36.3 ; 68.4	29.7 ; 68.2
Week 32		
N	32	56
Median	53.2	50.8
P25 ; P75	47.2 ; 58.4	43.8 ; 58.5
Mean (SD)	51.6 (10.9)	49.5 (10.3)
Min ; Max	17.5 ; 69.5	20.8 ; 63.1
Change from baseline to week 24		
N	24	42
Median	3.2	3.2
P25 ; P75	-5.3 ; 11.7	-1.7 ; 7.5
Mean (SD)	3.9 (11.3)	5.0 (10.6)
Min ; Max	-12.5 ; 37.9	-11.5 ; 34.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors,
OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis,
N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

80 PROMIS numeric rating scale v.1.0 - pain intensity 1a - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	43	25
Median	4.0	3.0
P25 ; P75	2.0 ; 5.0	1.0 ; 5.0
Mean (SD)	3.7 (2.6)	3.1 (2.9)
Min ; Max	0.0 ; 10.0	0.0 ; 10.0
Week 24		
N	57	31
Median	1.0	2.0
P25 ; P75	0.0 ; 3.0	0.0 ; 4.0
Mean (SD)	1.6 (2.1)	2.6 (2.4)
Min ; Max	0.0 ; 9.0	0.0 ; 8.0
Week 32		
N	57	29
Median	1.0	1.0
P25 ; P75	0.0 ; 3.0	0.0 ; 5.0
Mean (SD)	2.2 (2.5)	2.2 (2.8)
Min ; Max	0.0 ; 9.0	0.0 ; 9.0
Change from baseline to week 24		
N	39	23
Median	-1.0	0.0
P25 ; P75	-2.0 ; 0.0	-2.0 ; 1.0
Mean (SD)	-1.4 (2.2)	-0.5 (2.6)
Min ; Max	-6.0 ; 5.0	-8.0 ; 4.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

81 PROMIS numeric rating scale v.1.0 - pain intensity 1a - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	23	45
Median	3.0	4.0
P25 ; P75	0.0 ; 4.0	2.0 ; 5.0
Mean (SD)	3.0 (2.9)	3.7 (2.6)
Min ; Max	0.0 ; 10.0	0.0 ; 10.0
Week 24		
N	29	59
Median	0.0	2.0
P25 ; P75	0.0 ; 2.0	0.0 ; 4.0
Mean (SD)	1.1 (1.9)	2.4 (2.3)
Min ; Max	0.0 ; 8.0	0.0 ; 9.0
Week 32		
N	31	55
Median	0.0	2.0
P25 ; P75	0.0 ; 1.0	1.0 ; 5.0
Mean (SD)	1.3 (2.4)	2.7 (2.6)
Min ; Max	0.0 ; 8.0	0.0 ; 9.0
Change from baseline to week 24		
N	21	41
Median	-1.0	-1.0
P25 ; P75	-2.0 ; 0.0	-2.0 ; 0.0
Mean (SD)	-1.6 (2.8)	-0.8 (2.1)
Min ; Max	-8.0 ; 4.0	-5.0 ; 5.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

82 PROMIS short form v2.0 - upper extremity 7a - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	37	20
Median	39.8	36.7
P25 ; P75	35.7 ; 45.5	29.1 ; 43.7
Mean (SD)	41.7 (8.9)	37.4 (10.5)
Min ; Max	24.6 ; 58.2	23.0 ; 58.2
Week 24		
N	50	25
Median	46.3	43.4
P25 ; P75	40.7 ; 58.2	32.7 ; 46.0
Mean (SD)	46.5 (9.4)	42.6 (10.8)
Min ; Max	24.9 ; 58.2	24.1 ; 58.2
Week 32		
N	51	23
Median	47.3	44.4
P25 ; P75	39.0 ; 58.2	35.5 ; 58.2
Mean (SD)	47.0 (10.0)	43.9 (10.8)
Min ; Max	23.8 ; 58.2	26.0 ; 58.2
Change from baseline to week 24		
N	34	19
Median	1.9	0.0
P25 ; P75	0.0 ; 6.6	-3.4 ; 10.3
Mean (SD)	3.0 (6.6)	3.6 (7.7)
Min ; Max	-9.7 ; 20.8	-7.4 ; 16.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

83 PROMIS short form v2.0 - upper extremity 7a - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	21	36
Median	41.1	38.6
P25 ; P75	32.7 ; 44.8	32.8 ; 45.3
Mean (SD)	41.5 (10.8)	39.4 (9.0)
Min ; Max	23.0 ; 58.2	24.4 ; 58.2
Week 24		
N	27	48
Median	46.5	43.8
P25 ; P75	41.4 ; 58.2	37.8 ; 50.6
Mean (SD)	47.6 (10.8)	43.8 (9.4)
Min ; Max	24.9 ; 58.2	24.1 ; 58.2
Week 32		
N	29	45
Median	51.1	46.0
P25 ; P75	41.2 ; 58.2	37.5 ; 51.1
Mean (SD)	47.9 (11.2)	44.8 (9.6)
Min ; Max	23.8 ; 58.2	26.0 ; 58.2
Change from baseline to week 24		
N	20	33
Median	1.6	1.3
P25 ; P75	-0.1 ; 9.7	-2.3 ; 7.7
Mean (SD)	4.3 (7.8)	2.5 (6.4)
Min ; Max	-8.1 ; 20.8	-9.7 ; 16.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

84 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Total score - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	36	21
Median	38.9	42.9
P25 ; P75	28.9 ; 52.8	36.5 ; 67.7
Mean (SD)	41.1 (16.9)	49.1 (17.2)
Min ; Max	14.8 ; 80.8	23.3 ; 82.6
Week 24		
N	26	14
Median	30.8	23.1
P25 ; P75	20.0 ; 43.4	13.3 ; 41.7
Mean (SD)	32.7 (17.3)	27.2 (16.2)
Min ; Max	4.7 ; 62.8	6.7 ; 60.1
Week 32		
N	21	15
Median	32.6	25.0
P25 ; P75	18.8 ; 42.3	12.8 ; 35.2
Mean (SD)	34.5 (19.3)	25.9 (14.3)
Min ; Max	9.5 ; 84.4	8.3 ; 59.1
Change from baseline to week 24		
N	25	14
Median	-6.8	-17.3
P25 ; P75	-16.2 ; -2.4	-30.4 ; -0.7
Mean (SD)	-9.7 (18.2)	-18.7 (20.8)
Min ; Max	-51.1 ; 43.0	-57.9 ; 7.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

85 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Physical health - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	36	21
Median	40.0	65.0
P25 ; P75	27.5 ; 75.0	55.0 ; 80.0
Mean (SD)	46.5 (27.1)	65.0 (20.5)
Min ; Max	0.0 ; 95.0	15.0 ; 95.0
Week 24		
N	26	14
Median	27.5	22.5
P25 ; P75	10.0 ; 60.0	15.0 ; 50.0
Mean (SD)	34.4 (27.9)	30.0 (24.6)
Min ; Max	0.0 ; 95.0	0.0 ; 75.0
Week 32		
N	21	14
Median	25.0	22.5
P25 ; P75	20.0 ; 40.0	10.0 ; 45.0
Mean (SD)	30.2 (25.4)	29.3 (23.5)
Min ; Max	0.0 ; 85.0	0.0 ; 75.0
Change from baseline to week 24		
N	25	14
Median	-15.0	-32.5
P25 ; P75	-30.0 ; -2.5	-45.0 ; -10.0
Mean (SD)	-10.8 (32.3)	-33.9 (24.2)
Min ; Max	-50.0 ; 95.0	-75.0 ; 0.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

86 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Feeling - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	36	21
Median	31.3	37.5
P25 ; P75	12.5 ; 46.9	25.0 ; 68.8
Mean (SD)	35.1 (27.2)	44.6 (25.9)
Min ; Max	0.0 ; 100.0	12.5 ; 93.8
Week 24		
N	26	14
Median	25.0	15.6
P25 ; P75	6.3 ; 37.5	0.0 ; 25.0
Mean (SD)	28.1 (25.2)	17.4 (18.2)
Min ; Max	0.0 ; 87.5	0.0 ; 50.0
Week 32		
N	21	14
Median	18.8	9.4
P25 ; P75	6.3 ; 43.8	0.0 ; 18.8
Mean (SD)	26.2 (27.7)	13.4 (15.9)
Min ; Max	0.0 ; 93.8	0.0 ; 50.0
Change from baseline to week 24		
N	25	14
Median	-12.5	-18.8
P25 ; P75	-25.0 ; 0.0	-37.5 ; 0.0
Mean (SD)	-13.0 (25.6)	-21.4 (29.6)
Min ; Max	-68.8 ; 56.3	-87.5 ; 12.5

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

87 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - View of yourself - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	35	21
Median	45.0	45.0
P25 ; P75	40.0 ; 55.0	35.0 ; 70.0
Mean (SD)	48.0 (17.9)	50.2 (16.9)
Min ; Max	5.0 ; 85.0	25.0 ; 80.0
Week 24		
N	26	14
Median	47.5	25.0
P25 ; P75	25.0 ; 60.0	15.0 ; 50.0
Mean (SD)	44.2 (21.3)	28.6 (20.2)
Min ; Max	5.0 ; 95.0	0.0 ; 65.0
Week 32		
N	21	14
Median	50.0	27.5
P25 ; P75	25.0 ; 55.0	15.0 ; 50.0
Mean (SD)	44.8 (23.4)	31.3 (19.5)
Min ; Max	10.0 ; 95.0	0.0 ; 65.0
Change from baseline to week 24		
N	24	14
Median	0.0	-17.5
P25 ; P75	-20.0 ; 12.5	-35.0 ; 0.0
Mean (SD)	-3.8 (20.4)	-19.6 (22.3)
Min ; Max	-55.0 ; 30.0	-70.0 ; 5.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

88 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Sport and leisure - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	31	16
Median	75.0	85.0
P25 ; P75	62.5 ; 80.0	57.5 ; 94.4
Mean (SD)	66.5 (22.0)	76.1 (21.6)
Min ; Max	16.7 ; 95.0	40.0 ; 100.0
Week 24		
N	22	11
Median	52.5	45.0
P25 ; P75	35.0 ; 80.0	35.0 ; 83.3
Mean (SD)	51.4 (26.2)	54.1 (29.7)
Min ; Max	0.0 ; 95.0	0.0 ; 100.0
Week 32		
N	18	10
Median	65.0	50.0
P25 ; P75	33.3 ; 75.0	45.0 ; 68.8
Mean (SD)	56.6 (28.6)	58.2 (19.0)
Min ; Max	0.0 ; 100.0	40.0 ; 91.7
Change from baseline to week 24		
N	18	9
Median	-4.4	-15.0
P25 ; P75	-15.0 ; 0.0	-45.0 ; -5.0
Mean (SD)	-11.9 (19.7)	-20.7 (22.3)
Min ; Max	-62.5 ; 6.3	-48.8 ; 10.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

89 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Work and studies - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	32	14
Median	40.6	40.6
P25 ; P75	25.0 ; 56.3	18.8 ; 62.5
Mean (SD)	40.0 (23.3)	46.6 (27.8)
Min ; Max	0.0 ; 100.0	18.8 ; 100.0
Week 24		
N	23	8
Median	31.3	9.4
P25 ; P75	6.3 ; 43.8	0.0 ; 21.9
Mean (SD)	28.0 (21.6)	18.8 (29.3)
Min ; Max	0.0 ; 75.0	0.0 ; 87.5
Week 32		
N	19	10
Median	18.8	3.1
P25 ; P75	6.3 ; 50.0	0.0 ; 25.0
Mean (SD)	27.7 (27.5)	16.0 (28.9)
Min ; Max	0.0 ; 93.8	0.0 ; 91.7
Change from baseline to week 24		
N	22	7
Median	-6.3	-18.8
P25 ; P75	-25.0 ; 6.3	-50.0 ; -6.3
Mean (SD)	-13.9 (24.8)	-25.3 (21.8)
Min ; Max	-68.8 ; 25.0	-56.3 ; 0.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

90 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Dealing with haemophilia - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	36	21
Median	33.3	25.0
P25 ; P75	20.8 ; 41.7	16.7 ; 33.3
Mean (SD)	31.0 (18.3)	27.8 (20.6)
Min ; Max	0.0 ; 75.0	0.0 ; 100.0
Week 24		
N	26	14
Median	33.3	12.5
P25 ; P75	25.0 ; 50.0	0.0 ; 25.0
Mean (SD)	33.0 (20.7)	14.9 (17.4)
Min ; Max	0.0 ; 66.7	0.0 ; 58.3
Week 32		
N	20	15
Median	25.0	0.0
P25 ; P75	16.7 ; 37.5	0.0 ; 25.0
Mean (SD)	28.3 (21.0)	10.0 (13.8)
Min ; Max	0.0 ; 66.7	0.0 ; 33.3
Change from baseline to week 24		
N	25	14
Median	0.0	-8.3
P25 ; P75	-8.3 ; 16.7	-16.7 ; 0.0
Mean (SD)	-0.7 (23.6)	-12.5 (27.5)
Min ; Max	-50.0 ; 41.7	-100 ; 16.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

91 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Treatment - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	36	20
Median	37.5	34.4
P25 ; P75	23.4 ; 57.8	21.9 ; 59.4
Mean (SD)	41.2 (22.0)	40.3 (24.4)
Min ; Max	9.4 ; 90.6	9.4 ; 100.0
Week 24		
N	25	14
Median	28.1	14.1
P25 ; P75	12.5 ; 37.5	6.3 ; 31.3
Mean (SD)	27.9 (20.5)	17.2 (14.8)
Min ; Max	0.0 ; 68.8	0.0 ; 43.8
Week 32		
N	20	14
Median	26.6	15.6
P25 ; P75	14.1 ; 50.0	3.1 ; 34.4
Mean (SD)	31.3 (21.6)	18.3 (16.1)
Min ; Max	0.0 ; 78.1	0.0 ; 43.8
Change from baseline to week 24		
N	24	14
Median	-12.5	-17.2
P25 ; P75	-31.3 ; -4.7	-31.3 ; 0.0
Mean (SD)	-16.3 (27.4)	-17.9 (23.3)
Min ; Max	-87.5 ; 56.3	-59.4 ; 18.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

92 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Future - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	35	21
Median	40.0	50.0
P25 ; P75	20.0 ; 65.0	45.0 ; 65.0
Mean (SD)	45.2 (23.4)	53.6 (19.8)
Min ; Max	0.0 ; 95.0	10.0 ; 90.0
Week 24		
N	26	14
Median	35.0	30.0
P25 ; P75	20.0 ; 55.0	20.0 ; 55.0
Mean (SD)	38.5 (21.5)	37.9 (27.7)
Min ; Max	10.0 ; 80.0	5.0 ; 85.0
Week 32		
N	20	15
Median	40.0	25.0
P25 ; P75	22.5 ; 55.0	20.0 ; 65.0
Mean (SD)	41.5 (23.3)	34.7 (25.0)
Min ; Max	5.0 ; 90.0	5.0 ; 80.0
Change from baseline to week 24		
N	24	14
Median	-7.5	-10.0
P25 ; P75	-17.5 ; 0.0	-40.0 ; 10.0
Mean (SD)	-8.9 (23.2)	-15.4 (28.8)
Min ; Max	-70.0 ; 55.0	-70.0 ; 20.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

93 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Family planning - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	24	16
Median	15.6	41.7
P25 ; P75	0.0 ; 34.4	8.3 ; 58.3
Mean (SD)	19.7 (21.4)	35.7 (26.9)
Min ; Max	0.0 ; 75.0	0.0 ; 75.0
Week 24		
N	15	8
Median	0.0	0.0
P25 ; P75	0.0 ; 18.8	0.0 ; 47.9
Mean (SD)	11.8 (16.5)	24.5 (38.2)
Min ; Max	0.0 ; 50.0	0.0 ; 100.0
Week 32		
N	12	8
Median	0.0	0.0
P25 ; P75	0.0 ; 18.8	0.0 ; 25.0
Mean (SD)	10.9 (15.8)	14.1 (24.3)
Min ; Max	0.0 ; 50.0	0.0 ; 62.5
Change from baseline to week 24		
N	12	8
Median	0.0	-16.7
P25 ; P75	-18.8 ; 3.1	-41.7 ; 6.3
Mean (SD)	-6.6 (16.1)	-15.4 (30.1)
Min ; Max	-37.5 ; 14.6	-50.0 ; 31.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

94 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Partnership and sexuality - >= 17 years - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	55	28
N in FAS and ADS	47	23
Baseline		
N	35	21
Median	16.7	25.0
P25 ; P75	0.0 ; 25.0	8.3 ; 50.0
Mean (SD)	19.0 (19.3)	32.9 (31.3)
Min ; Max	0.0 ; 75.0	0.0 ; 100.0
Week 24		
N	26	14
Median	4.2	8.3
P25 ; P75	0.0 ; 16.7	0.0 ; 25.0
Mean (SD)	15.7 (23.7)	25.0 (34.9)
Min ; Max	0.0 ; 83.3	0.0 ; 100.0
Week 32		
N	21	15
Median	25.0	0.0
P25 ; P75	0.0 ; 41.7	0.0 ; 33.3
Mean (SD)	25.4 (27.6)	22.2 (33.0)
Min ; Max	0.0 ; 91.7	0.0 ; 100.0
Change from baseline to week 24		
N	25	14
Median	0.0	0.0
P25 ; P75	-25.0 ; 8.3	-16.7 ; 8.3
Mean (SD)	-4.0 (21.4)	-7.7 (39.6)
Min ; Max	-41.7 ; 50.0	-83.3 ; 50.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum. P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

95 Haemophilia treament experience measure (Hemo-TEM) - Total score - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	22.2	19.8
P25 ; P75	10.7 ; 35.1	10.6 ; 43.6
Mean (SD)	23.6 (17.4)	30.1 (24.4)
Min ; Max	0.0 ; 71.3	2.9 ; 85.5
Week 24		
N	57	31
Median	5.0	5.0
P25 ; P75	2.5 ; 10.6	1.7 ; 14.1
Mean (SD)	8.8 (10.1)	9.1 (9.6)
Min ; Max	0.0 ; 44.3	0.0 ; 31.4
Week 32		
N	56	29
Median	7.2	5.0
P25 ; P75	3.2 ; 13.1	1.7 ; 10.8
Mean (SD)	9.0 (8.4)	7.6 (8.6)
Min ; Max	0.0 ; 40.8	0.0 ; 32.3
Change from baseline to week 24		
N	38	23
Median	-10.2	-10.0
P25 ; P75	-25.5 ; -0.7	-45.2 ; 0.5
Mean (SD)	-15.2 (18.6)	-19.4 (27.4)
Min ; Max	-67.3 ; 13.2	-81.3 ; 10.5

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

96 Haemophilia treament experience measure (Hemo-TEM) - Injection difficulties - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	16.7	20.8
P25 ; P75	0.0 ; 33.3	4.2 ; 50.0
Mean (SD)	23.2 (27.5)	29.2 (26.9)
Min ; Max	0.0 ; 100.0	0.0 ; 91.7
Week 24		
N	57	31
Median	0.0	8.3
P25 ; P75	0.0 ; 8.3	0.0 ; 8.3
Mean (SD)	8.5 (14.0)	7.5 (9.9)
Min ; Max	0.0 ; 75.0	0.0 ; 41.7
Week 32		
N	56	29
Median	0.0	0.0
P25 ; P75	0.0 ; 8.3	0.0 ; 8.3
Mean (SD)	6.8 (13.4)	8.0 (14.5)
Min ; Max	0.0 ; 75.0	0.0 ; 50.0
Change from baseline to week 24		
N	38	23
Median	-8.3	-8.3
P25 ; P75	-25.0 ; 0.0	-41.7 ; 0.0
Mean (SD)	-14.9 (31.2)	-21.7 (28.7)
Min ; Max	-100 ; 50.0	-83.3 ; 25.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

97 Haemophilia treament experience measure (Hemo-TEM) - Physical impact - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	20.8	29.2
P25 ; P75	12.5 ; 33.3	20.8 ; 47.9
Mean (SD)	23.5 (16.6)	33.2 (20.9)
Min ; Max	0.0 ; 75.0	0.0 ; 79.2
Week 24		
N	57	31
Median	8.3	8.3
P25 ; P75	0.0 ; 16.7	0.0 ; 20.8
Mean (SD)	11.7 (13.8)	12.6 (12.6)
Min ; Max	0.0 ; 54.2	0.0 ; 50.0
Week 32		
N	56	29
Median	8.3	8.3
P25 ; P75	2.1 ; 22.9	4.2 ; 16.7
Mean (SD)	14.1 (13.7)	12.4 (12.0)
Min ; Max	0.0 ; 58.3	0.0 ; 45.8
Change from baseline to week 24		
N	38	23
Median	-6.3	-8.3
P25 ; P75	-20.8 ; 4.2	-41.7 ; 0.0
Mean (SD)	-12.0 (19.6)	-17.8 (22.9)
Min ; Max	-66.7 ; 12.5	-62.5 ; 8.3

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

98 Haemophilia treament experience measure (Hemo-TEM) - Interference - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	25.0	25.0
P25 ; P75	0.0 ; 50.0	9.4 ; 50.0
Mean (SD)	26.9 (25.9)	34.4 (32.6)
Min ; Max	0.0 ; 93.8	0.0 ; 100.0
Week 24		
N	57	31
Median	0.0	0.0
P25 ; P75	0.0 ; 12.5	0.0 ; 12.5
Mean (SD)	5.4 (8.9)	8.3 (11.7)
Min ; Max	0.0 ; 31.3	0.0 ; 41.7
Week 32		
N	56	29
Median	0.0	0.0
P25 ; P75	0.0 ; 12.5	0.0 ; 6.3
Mean (SD)	5.7 (8.9)	5.1 (10.0)
Min ; Max	0.0 ; 31.3	0.0 ; 37.5
Change from baseline to week 24		
N	38	23
Median	-18.8	-12.5
P25 ; P75	-37.5 ; 0.0	-50.0 ; 0.0
Mean (SD)	-22.1 (26.8)	-25.4 (37.9)
Min ; Max	-93.8 ; 18.8	-100 ; 18.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

99 Haemophilia treament experience measure (Hemo-TEM) - Treatment bother - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	16.1	14.3
P25 ; P75	3.6 ; 32.1	1.8 ; 39.3
Mean (SD)	21.9 (20.6)	25.7 (29.8)
Min ; Max	0.0 ; 85.7	0.0 ; 92.9
Week 24		
N	57	31
Median	3.6	0.0
P25 ; P75	0.0 ; 10.7	0.0 ; 7.1
Mean (SD)	8.0 (11.1)	6.9 (16.1)
Min ; Max	0.0 ; 46.4	0.0 ; 85.7
Week 32		
N	56	29
Median	3.6	0.0
P25 ; P75	0.0 ; 10.7	0.0 ; 3.6
Mean (SD)	7.5 (9.2)	3.3 (6.2)
Min ; Max	0.0 ; 39.3	0.0 ; 21.4
Change from baseline to week 24		
N	38	23
Median	-8.9	-7.1
P25 ; P75	-28.6 ; 0.0	-35.7 ; 0.0
Mean (SD)	-14.5 (22.8)	-17.4 (36.8)
Min ; Max	-82.1 ; 25.0	-92.9 ; 85.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

100 Haemophilia treament experience measure (Hemo-TEM) - Emotional impact - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Baseline		
N	42	24
Median	16.7	20.8
P25 ; P75	4.2 ; 37.5	6.3 ; 41.7
Mean (SD)	22.3 (21.7)	28.0 (26.5)
Min ; Max	0.0 ; 75.0	0.0 ; 100.0
Week 24		
N	57	31
Median	4.2	0.0
P25 ; P75	0.0 ; 16.7	0.0 ; 12.5
Mean (SD)	10.7 (14.3)	9.9 (16.2)
Min ; Max	0.0 ; 55.0	0.0 ; 50.0
Week 32		
N	56	29
Median	4.2	4.2
P25 ; P75	0.0 ; 20.8	0.0 ; 16.7
Mean (SD)	11.0 (12.5)	9.4 (13.6)
Min ; Max	0.0 ; 37.5	0.0 ; 50.0
Change from baseline to week 24		
N	38	23
Median	-8.3	0.0
P25 ; P75	-16.7 ; 0.0	-41.7 ; 4.2
Mean (SD)	-12.4 (19.2)	-14.7 (32.2)
Min ; Max	-70.8 ; 25.0	-100 ; 20.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

101 Haemophilia treament experience measure (Hemo-TEM) - Total score - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	13.5	22.9
P25 ; P75	5.8 ; 35.1	12.3 ; 37.0
Mean (SD)	23.4 (21.8)	27.2 (19.6)
Min ; Max	1.7 ; 85.5	0.0 ; 78.1
Week 24		
N	29	59
Median	3.3	5.7
P25 ; P75	1.7 ; 9.2	2.5 ; 13.6
Mean (SD)	7.5 (9.3)	9.6 (10.2)
Min ; Max	0.0 ; 36.0	0.0 ; 44.3
Week 32		
N	30	55
Median	3.3	7.5
P25 ; P75	0.8 ; 12.5	3.4 ; 13.5
Mean (SD)	7.3 (8.8)	9.3 (8.2)
Min ; Max	0.0 ; 40.8	0.0 ; 33.1
Change from baseline to week 24		
N	21	40
Median	-5.8	-11.1
P25 ; P75	-24.3 ; -2.4	-30.4 ; -0.2
Mean (SD)	-14.9 (22.2)	-17.7 (22.4)
Min ; Max	-81.3 ; 13.2	-68.7 ; 10.5

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

102 Haemophilia treament experience measure (Hemo-TEM) - Injection difficulties - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	8.3	16.7
P25 ; P75	8.3 ; 41.7	0.0 ; 37.5
Mean (SD)	25.4 (29.3)	25.4 (26.5)
Min ; Max	0.0 ; 100.0	0.0 ; 100.0
Week 24		
N	29	59
Median	0.0	0.0
P25 ; P75	0.0 ; 16.7	0.0 ; 8.3
Mean (SD)	7.5 (9.5)	8.5 (14.0)
Min ; Max	0.0 ; 33.3	0.0 ; 75.0
Week 32		
N	30	55
Median	0.0	0.0
P25 ; P75	0.0 ; 16.7	0.0 ; 8.3
Mean (SD)	9.7 (17.1)	5.9 (11.4)
Min ; Max	0.0 ; 75.0	0.0 ; 50.0
Change from baseline to week 24		
N	21	40
Median	-8.3	-8.3
P25 ; P75	-41.7 ; 8.3	-29.2 ; 0.0
Mean (SD)	-16.7 (29.9)	-17.9 (30.8)
Min ; Max	-75.0 ; 25.0	-100 ; 50.0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

103 Haemophilia treament experience measure (Hemo-TEM) - Physical impact - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	20.8	25.0
P25 ; P75	8.3 ; 33.3	16.7 ; 37.5
Mean (SD)	24.6 (19.6)	28.2 (18.4)
Min ; Max	0.0 ; 75.0	0.0 ; 79.2
Week 24		
N	29	59
Median	4.2	8.3
P25 ; P75	0.0 ; 12.5	4.2 ; 20.8
Mean (SD)	8.6 (10.7)	13.7 (14.2)
Min ; Max	0.0 ; 41.7	0.0 ; 54.2
Week 32		
N	30	55
Median	8.3	12.5
P25 ; P75	0.0 ; 12.5	4.2 ; 25.0
Mean (SD)	9.6 (12.5)	15.6 (13.0)
Min ; Max	0.0 ; 58.3	0.0 ; 50.0
Change from baseline to week 24		
N	21	40
Median	-8.3	-6.3
P25 ; P75	-33.3 ; 0.0	-20.8 ; 0.0
Mean (SD)	-15.1 (22.9)	-13.6 (20.1)
Min ; Max	-62.5 ; 12.5	-66.7 ; 12.5

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

104 Haemophilia treament experience measure (Hemo-TEM) - Interference - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	12.5	25.0
P25 ; P75	0.0 ; 50.0	9.4 ; 50.0
Mean (SD)	27.0 (30.7)	30.9 (27.6)
Min ; Max	0.0 ; 100.0	0.0 ; 100.0
Week 24		
N	29	59
Median	0.0	0.0
P25 ; P75	0.0 ; 12.5	0.0 ; 12.5
Mean (SD)	6.4 (11.1)	6.4 (9.5)
Min ; Max	0.0 ; 41.7	0.0 ; 31.3
Week 32		
N	30	55
Median	0.0	0.0
P25 ; P75	0.0 ; 0.0	0.0 ; 8.3
Mean (SD)	4.8 (10.2)	5.9 (8.7)
Min ; Max	0.0 ; 37.5	0.0 ; 33.3
Change from baseline to week 24		
N	21	40
Median	-6.3	-18.8
P25 ; P75	-31.3 ; 0.0	-39.6 ; 0.0
Mean (SD)	-19.4 (32.6)	-25.4 (30.6)
Min ; Max	-100 ; 18.8	-100 ; 18.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

105 Haemophilia treament experience measure (Hemo-TEM) - Treatment bother - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	10.7	17.9
P25 ; P75	3.6 ; 25.0	3.6 ; 39.3
Mean (SD)	16.4 (19.7)	26.7 (25.6)
Min ; Max	0.0 ; 85.7	0.0 ; 92.9
Week 24		
N	29	59
Median	3.6	3.6
P25 ; P75	0.0 ; 7.1	0.0 ; 10.7
Mean (SD)	8.7 (13.3)	7.0 (12.9)
Min ; Max	0.0 ; 46.4	0.0 ; 85.7
Week 32		
N	30	55
Median	3.6	3.6
P25 ; P75	0.0 ; 7.1	0.0 ; 10.7
Mean (SD)	4.6 (6.9)	6.9 (9.2)
Min ; Max	0.0 ; 28.6	0.0 ; 39.3
Change from baseline to week 24		
N	21	40
Median	0.0	-14.3
P25 ; P75	-7.1 ; 3.6	-33.9 ; 0.0
Mean (SD)	-7.3 (21.9)	-19.9 (30.9)
Min ; Max	-85.7 ; 25.0	-92.9 ; 85.7

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

106 Haemophilia treament experience measure (Hemo-TEM) - Emotional impact - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Baseline		
N	22	44
Median	12.5	20.8
P25 ; P75	0.0 ; 41.7	8.3 ; 37.5
Mean (SD)	23.9 (28.6)	24.6 (20.9)
Min ; Max	0.0 ; 100.0	0.0 ; 83.3
Week 24		
N	29	59
Median	0.0	8.3
P25 ; P75	0.0 ; 8.3	0.0 ; 20.8
Mean (SD)	6.5 (12.4)	12.4 (15.7)
Min ; Max	0.0 ; 50.0	0.0 ; 55.0
Week 32		
N	30	55
Median	2.1	4.2
P25 ; P75	0.0 ; 12.5	0.0 ; 20.8
Mean (SD)	7.5 (11.2)	12.0 (13.4)
Min ; Max	0.0 ; 37.5	0.0 ; 50.0
Change from baseline to week 24		
N	21	40
Median	-12.5	-4.2
P25 ; P75	-20.8 ; 0.0	-16.7 ; 0.0
Mean (SD)	-16.1 (26.4)	-11.8 (23.9)
Min ; Max	-100 ; 25.0	-83.3 ; 20.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

107 Haemophilia patient preference questionnaire (H-PPQ) - by haemophilia type - week 24 - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
1. Overall, which treatment do you prefer?		
Current treatment	47 (75.8)	30 (81.1)
Previous treatment	1 (1.6)	0
No preference	4 (6.5)	1 (2.7)
Missing	10 (16.1)	6 (16.2)
For subjects preferring current treatment:		
N preferring current treatment	47 (100)	30 (100)
2. How strong is this treatment preference (indicated in question 1)?		
Very strong	30 (63.8)	22 (73.3)
Fairly strong	14 (29.8)	8 (26.7)
Not very strong	3 (6.4)	0
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	13 (27.7)	4 (13.3)
Feels less emotionally distressing	9 (19.1)	3 (10.0)
Less painful to inject	18 (38.3)	7 (23.3)
How often do you have to inject	4 (8.5)	2 (6.7)
Fewer bleeds	32 (68.1)	26 (86.7)
Require less time	21 (44.7)	12 (40.0)
Other reason	3 (6.4)	0
For subjects preferring previous treatment:		
N preferring previous treatment	1 (100)	0
2. How strong is this treatment preference (indicated in question 1)?		

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

Haemophilia patient preference questionnaire (H-PPQ) - by haemophilia type - week 24 - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
Very strong	1 (100)	0
Fairly strong	0	0
Not very strong	0	0
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	0	0
Feels less emotionally distressing	1 (100)	0
Less painful to inject	1 (100)	0
How often do you have to inject	0	0
Fewer bleeds	0	0
Require less time	0	0
Other reason	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

108 Haemophilia patient preference questionnaire (H-PPQ) - by age group - week 24 - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
1. Overall, which treatment do you prefer?		
Current treatment	26 (76.5)	51 (78.5)
Previous treatment	1 (2.9)	0
No preference	1 (2.9)	4 (6.2)
Missing	6 (17.6)	10 (15.4)
For subjects preferring current treatment:		
N preferring current treatment	26 (100)	51 (100)
2. How strong is this treatment preference (indicated in question 1)?		
Very strong	20 (76.9)	32 (62.7)
Fairly strong	5 (19.2)	17 (33.3)
Not very strong	1 (3.8)	2 (3.9)
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	8 (30.8)	9 (17.6)
Feels less emotionally distressing	6 (23.1)	6 (11.8)
Less painful to inject	11 (42.3)	14 (27.5)
How often do you have to inject	2 (7.7)	4 (7.8)
Fewer bleeds	19 (73.1)	39 (76.5)
Require less time	10 (38.5)	23 (45.1)
Other reason	0	3 (5.9)
For subjects preferring previous treatment:		
N preferring previous treatment	1 (100)	0
2. How strong is this treatment preference (indicated in question 1)?		

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

Haemophilia patient preference questionnaire (H-PPQ) - by age group - week 24 - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
Very strong	1 (100)	0
Fairly strong	0	0
Not very strong	0	0
3. What are the TWO main reasons for this treatment preference?		
Easier to remember to inject	0	0
Feels less emotionally distressing	1 (100)	0
Less painful to inject	1 (100)	0
How often do you have to inject	0	0
Fewer bleeds	0	0
Require less time	0	0
Other reason	0	0

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.

109 Patient global impression of severity (PGI-S) - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Level of physical functioning over the past week		
Baseline		
N	38 (100)	24 (100)
Very good	4 (10.5)	1 (4.2)
Good	15 (39.5)	6 (25.0)
Fair	10 (26.3)	10 (41.7)
Poor	5 (13.2)	2 (8.3)
Very poor	4 (10.5)	5 (20.8)
Week 4		
N	39 (100)	24 (100)
Very good	11 (28.2)	4 (16.7)
Good	16 (41.0)	10 (41.7)
Fair	10 (25.6)	8 (33.3)
Poor	2 (5.1)	2 (8.3)
Week 8		
N	51 (100)	28 (100)
Very good	16 (31.4)	6 (21.4)
Good	20 (39.2)	11 (39.3)
Fair	10 (19.6)	10 (35.7)
Poor	5 (9.8)	
Very poor		1 (3.6)
Week 16		
N	46 (100)	28 (100)
Very good	15 (32.6)	7 (25.0)
Good	19 (41.3)	11 (39.3)
Fair	9 (19.6)	8 (28.6)
Poor	3 (6.5)	2 (7.1)
Week 24		
N	52 (100)	31 (100)
Very good	16 (30.8)	6 (19.4)
Good	18 (34.6)	16 (51.6)
Fair	15 (28.8)	7 (22.6)
Poor	3 (5.8)	2 (6.5)
Week 32		
N	51 (100)	29 (100)
Very good	15 (29.4)	10 (34.5)
Good	17 (33.3)	9 (31.0)
Fair	16 (31.4)	8 (27.6)
Poor	2 (3.9)	1 (3.4)
Very poor	1 (2.0)	1 (3.4)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

110 Patient global impression of severity (PGI-S) - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Level of physical functioning over the past week		
Baseline		
N	21 (100)	41 (100)
Very good	3 (14.3)	2 (4.9)
Good	10 (47.6)	11 (26.8)
Fair	7 (33.3)	13 (31.7)
Poor		7 (17.1)
Very poor	1 (4.8)	8 (19.5)
Week 4		
N	20 (100)	43 (100)
Very good	8 (40.0)	7 (16.3)
Good	7 (35.0)	19 (44.2)
Fair	4 (20.0)	14 (32.6)
Poor	1 (5.0)	3 (7.0)
Week 8		
N	27 (100)	52 (100)
Very good	11 (40.7)	11 (21.2)
Good	11 (40.7)	20 (38.5)
Fair	5 (18.5)	15 (28.8)
Poor		5 (9.6)
Very poor		1 (1.9)
Week 16		
N	28 (100)	46 (100)
Very good	12 (42.9)	10 (21.7)
Good	13 (46.4)	17 (37.0)
Fair	3 (10.7)	14 (30.4)
Poor		5 (10.9)
Week 24		
N	28 (100)	55 (100)
Very good	12 (42.9)	10 (18.2)
Good	14 (50.0)	20 (36.4)
Fair	2 (7.1)	20 (36.4)
Poor		5 (9.1)
Week 32		
N	29 (100)	51 (100)
Very good	17 (58.6)	8 (15.7)
Good	10 (34.5)	16 (31.4)
Fair	2 (6.9)	22 (43.1)
Poor		3 (5.9)
Very poor		2 (3.9)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

111 Patient global impression of change (PGI-C) - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
N in FAS	71	43
N in FAS and ADS	62	37
Overall change in your level of physical functioning since you started taking the study medication		
Week 4		
N	39 (100)	23 (100)
Very much better	12 (30.8)	12 (52.2)
Moderately better	21 (53.8)	3 (13.0)
A little better	5 (12.8)	5 (21.7)
No change	1 (2.6)	3 (13.0)
Week 8		
N	51 (100)	27 (100)
Very much better	25 (49.0)	14 (51.9)
Moderately better	15 (29.4)	6 (22.2)
A little better	7 (13.7)	4 (14.8)
No change	3 (5.9)	3 (11.1)
Moderately worse	1 (2.0)	
Week 16		
N	45 (100)	28 (100)
Very much better	27 (60.0)	12 (42.9)
Moderately better	14 (31.1)	10 (35.7)
A little better	3 (6.7)	5 (17.9)
No change	1 (2.2)	1 (3.6)
Week 24		
N	52 (100)	31 (100)
Very much better	26 (50.0)	20 (64.5)
Moderately better	18 (34.6)	6 (19.4)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

Patient global impression of change (PGI-C) - by haemophilia type - descriptive statistics - HAwI and HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Haemophilia A	Haemophilia B
A little better	5 (9.6)	3 (9.7)
No change	3 (5.8)	2 (6.5)
Week 32		
N	51 (100)	29 (100)
Very much better	29 (56.9)	18 (62.1)
Moderately better	15 (29.4)	7 (24.1)
A little better	4 (7.8)	2 (6.9)
No change	1 (2.0)	2 (6.9)
A little worse	2 (3.9)	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

112 Patient global impression of change (PGI-C) - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
N in FAS	36	78
N in FAS and ADS	34	65
Overall change in your level of physical functioning since you started taking the study medication		
Week 4		
N	20 (100)	42 (100)
Very much better	8 (40.0)	16 (38.1)
Moderately better	8 (40.0)	16 (38.1)
A little better	3 (15.0)	7 (16.7)
No change	1 (5.0)	3 (7.1)
Week 8		
N	27 (100)	51 (100)
Very much better	19 (70.4)	20 (39.2)
Moderately better	5 (18.5)	16 (31.4)
A little better	3 (11.1)	8 (15.7)
No change		6 (11.8)
Moderately worse		1 (2.0)
Week 16		
N	28 (100)	45 (100)
Very much better	18 (64.3)	21 (46.7)
Moderately better	9 (32.1)	15 (33.3)
A little better	1 (3.6)	7 (15.6)
No change		2 (4.4)
Week 24		
N	28 (100)	55 (100)
Very much better	20 (71.4)	26 (47.3)
Moderately better	7 (25.0)	17 (30.9)
A little better		8 (14.5)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

Patient global impression of change (PGI-C) - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2-4)	
	Adolescents	Adults
No change	1 (3.6)	4 (7.3)
Week 32		
N	29 (100)	51 (100)
Very much better	22 (75.9)	25 (49.0)
Moderately better	6 (20.7)	16 (31.4)
A little better	1 (3.4)	5 (9.8)
No change		3 (5.9)
A little worse		2 (3.9)

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
Baseline is defined as visit 2a for concizumab PPX (arms 2, 3 and 4). Week numbers are relative to the relevant baseline.

113 Physical activity - change from baseline to end of main - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2 and 4)	
	Adolescents	Adults
N in FAS	36	57
N in FAS and ADS	34	50
Change in light activity relative to awake time (%)		
N	21	35
Median	-2.4	-0.4
P25 ; P75	-3.4 ; 2.7	-4.1 ; 1.1
Mean (SD)	-1.3 (5.0)	-2.0 (5.4)
Min ; Max	-12.7 ; 4.9	-20.7 ; 5.2
Change in moderate activity relative to awake time (%)		
N	21	35
Median	0.7	0.7
P25 ; P75	-2.6 ; 2.6	-1.2 ; 3.7
Mean (SD)	0.9 (4.6)	2.2 (5.2)
Min ; Max	-4.3 ; 13.9	-4.4 ; 20.6
Change in vigorous activity relative to awake time (%)		
N	21	35
Median	0.1	-0.0
P25 ; P75	-0.4 ; 1.2	-0.3 ; 0.1
Mean (SD)	0.3 (1.2)	-0.1 (0.6)
Min ; Max	-1.4 ; 2.8	-2.0 ; 1.2
Change in moderate or vigorous activity relative to awake time (%)		
N	21	35
Median	2.4	0.4
P25 ; P75	-2.7 ; 3.4	-1.1 ; 4.1
Mean (SD)	1.3 (5.0)	2.0 (5.4)
Min ; Max	-4.9 ; 12.7	-5.2 ; 20.7
Change in steps relative to awake time (steps/hour)		
N	21	35
Median	67.2	30.6
P25 ; P75	-35.1 ; 131.6	-2.6 ; 100.7
Mean (SD)	40.0 (167.7)	60.1 (147.1)
Min ; Max	-363.1 ; 458.8	-309.9 ; 424.4
Change in vector magnitude counts relative to awake time (counts/min)		
N	21	35
Median	-54.9	86.6
P25 ; P75	-351.5 ; 216.3	-242.4 ; 287.2
Mean (SD)	-187.2 (661.8)	493.0 (2248.8)
Min ; Max	-2179.0 ; 779.3	-523.6 ; 13032.1

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.

Physical activity - change from baseline to end of main - by age group - descriptive statistics - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	Concizumab PPX (arms 2 and 4)	
	Adolescents	Adults
Change in sedentary time relative to awake time (%)		
N	21	35
Median	1.8	-1.5
P25 ; P75	-0.4 ; 6.9	-4.5 ; 3.8
Mean (SD)	4.9 (9.9)	-2.1 (8.4)
Min ; Max	-5.6 ; 40.2	-37.2 ; 8.2
Change in non-sedentary time relative to awake time (%)		
N	21	35
Median	-1.8	1.5
P25 ; P75	-6.9 ; 0.4	-3.8 ; 4.5
Mean (SD)	-4.9 (9.9)	2.1 (8.4)
Min ; Max	-40.2 ; 5.6	-8.2 ; 37.2
Change in awake time (min)		
N	21	36
Median	-23.1	-42.4
P25 ; P75	-92.3 ; 48.5	-173.4 ; 59.4
Mean (SD)	-58.4 (234.0)	-62.3 (206.9)
Min ; Max	-736.5 ; 377.9	-641.7 ; 295.8
Change in sleep time (min)		
N	21	36
Median	-42.2	-45.8
P25 ; P75	-79.3 ; 31.1	-188.6 ; 17.2
Mean (SD)	-8.6 (235.0)	-66.8 (216.4)
Min ; Max	-378.6 ; 615.0	-564.0 ; 582.9
Change in wear time (min)		
N	21	36
Median	-26.1	-26.6
P25 ; P75	-236.1 ; 52.0	-279.2 ; 31.9
Mean (SD)	-67.1 (383.8)	-129.1 (341.8)
Min ; Max	-779.4 ; 661.1	-1027.7 ; 589.9
Change in non-wear time (min)		
N	21	36
Median	12.2	22.4
P25 ; P75	-0.0 ; 99.3	-34.6 ; 247.8
Mean (SD)	51.4 (361.1)	133.5 (312.4)
Min ; Max	-630.0 ; 805.6	-530.3 ; 1031.1

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, SD: standard deviation, Min: minimum, Max: maximum.
P25/P75 is the 25th/75th percentile.

114 Haemophilia treatment experience measure (Hemo-TEM) - Total score - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analysis se t - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	32.2		12.3
95% CI	[19.84,44.53]		[5.54,18.96]
Mean CfB score estimate at week 24	3.0		-17.0
95% CI	[-9.36,15.33]		[-23.66,-10.25]
Difference estimate at week 24		-19.94	
95% CI		[-34.31,-5.57]	
p-value		0.009	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

115 Haemophilia treatment experience measure (Hemo-TEM) - Injection difficulties - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	45.3		12.5
95% CI	[29.54,60.98]		[3.91,21.02]
Mean CfB score estimate at week 24	7.6		-25.2
95% CI	[-8.13,23.32]		[-33.76,-16.65]
Difference estimate at week 24		-32.80	
95% CI		[-51.09,-14.51]	
p-value		0.001	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

116 Haemophilia treatment experience measure (Hemo-TEM) - Physical impact - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analys is set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	22.8		14.3
95% CI	[8.04,37.48]		[6.69,21.91]
Mean CfB score estimate at week 24	-5.6		-14.0
95% CI	[-20.29,9.14]		[-21.64,-6.42]
Difference estimate at week 24		-8.46	
95% CI		[-25.92,9.01]	
p-value		0.325	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

117 Haemophilia treatment experience measure (Hemo-TEM) - Interference - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	33.9		11.6
95% CI	[15.96,51.83]		[1.78,21.33]
Mean CfB score estimate at week 24	3.6		-18.7
95% CI	[-14.29,21.58]		[-28.47,-8.92]
Difference estimate at week 24		-22.34	
95% CI		[-43.19,-1.49]	
p-value		0.037	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

118 Haemophilia treatment experience measure (Hemo-TEM) - Treatment bother - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analy sis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	23.2		10.4
95% CI	[10.44,35.87]		[3.43,17.28]
Mean CfB score estimate at week 24	0.7		-12.1
95% CI	[-11.99,13.44]		[-19.00,-5.15]
Difference estimate at week 24		-12.80	
95% CI		[-27.59,1.99]	
p-value		0.086	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

119 Haemophilia treatment experience measure (Hemo-TEM) - Emotional impact - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analy sis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
N contributing to analysis	6		19
Mean score estimate at week 24	34.2		13.1
95% CI	[20.10,48.32]		[5.41,20.79]
Mean CfB score estimate at week 24	6.9		-14.2
95% CI	[-7.23,20.99]		[-21.93,-6.54]
Difference estimate at week 24		-21.11	
95% CI		[-37.51,-4.71]	
p-value		0.014	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

120 Haemophilia treatment experience measure (Hemo-TEM) - change in total score - <=-8.0 - summary - HAwI+HBwI - OTexIR - full analysis set - t rial 4311

	No PPX	Concizumab PPX			
	Arm 1 N (%)	Arm 2 N (%)	Arm 3 N (%)	Arm 4 N (%)	Arms 2-4 N (%)
N in FAS	19	33	21	60	114
N in FAS and ADS	19	29	15	55	99
Total score <=-8.0					
Week 24					
N	6	19	12	30	61
Yes	1 (16.7)	11 (57.9)	5 (41.7)	18 (60.0)	34 (55.7)
No	5 (83.3)	8 (42.1)	7 (58.3)	12 (40.0)	27 (44.3)
Week 32					
N	0	21	11	26	58
Yes	0	13 (61.9)	3 (27.3)	18 (69.2)	34 (58.6)
No	0	8 (38.1)	8 (72.7)	8 (30.8)	24 (41.4)

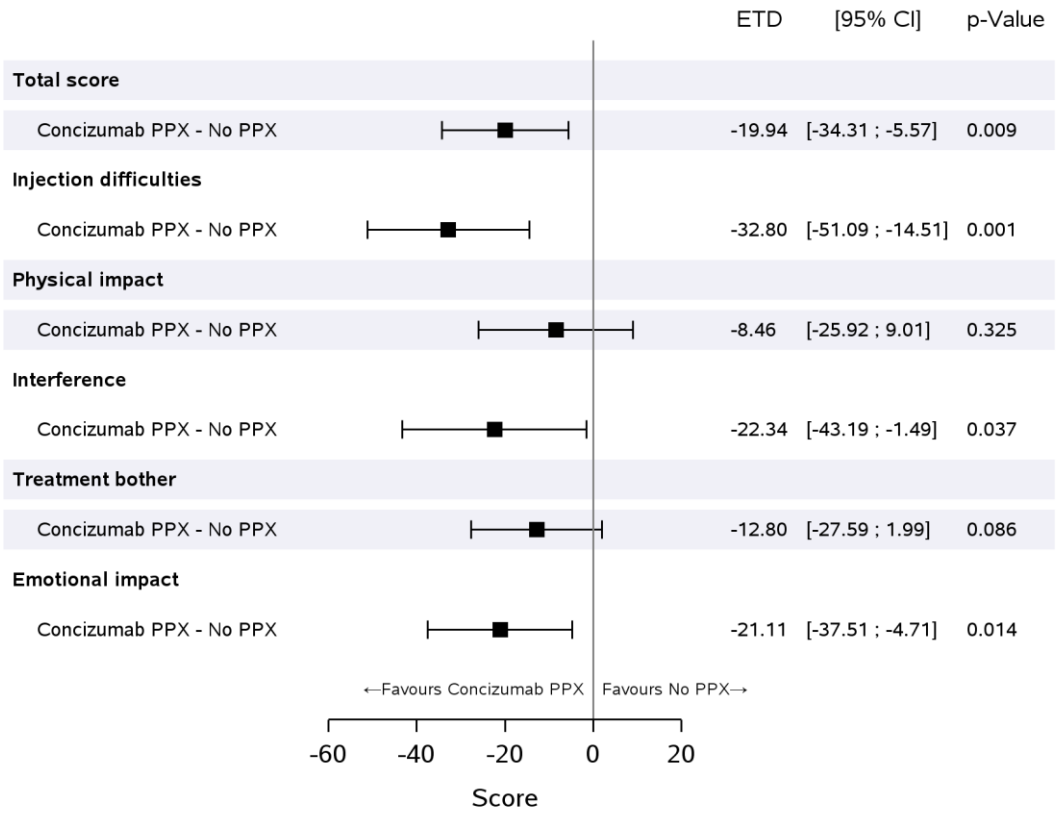
HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
%: Proportion of subjects with non-missing information.

121 Haemophilia treatment experience measure (Hemo-TEM) - change in total score - <=-8.0 - week 24 - statistical analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
Total score <= -8.0			
Odds estimate	0.1		2.6
95% CI	[0.00,1.64]		[0.55,12.31]
Odds ratio		42.55	
95% CI		[1.05,1730.79]	
p-value		0.047	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CI: Confidence interval.
p-values are for two-sided tests of no difference from 1.
The assessment is derived as a dichotomisation of change from baseline to week 24. The number of subjects having a change from baseline greater or equal to 8.0 is analysed using a logistic regression model with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline score as a covariate.

122 Haemophilia treatment experience measure (Hemo-TEM) - week 24 - forest plot - statistica l analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311



HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, ETD: estimated treatment difference, CI: Confidence interval. P-values are for two-sided tests of no difference from 0.
Change from baseline values have been analysed using an analysis of covariance (ANCOVA), with treatment, type of haemophilia and bleeding frequency prior to screening as factors, and baseline value as a covariate.

nn7415/nn7415-summary/efficacy_fda_nda_20220527_er
27MAY2022:13:58:36 - f-hemotemforest.sas/f-hemotemforest.png

123 Bleeding episodes - Japanese subjects - listing - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

Trial/ Subject ID/ Arm	Age (years)/ Haemophilia type	Onset/ Resolution	Period	Study day/ Duration (days)	Cause of bleed/ Classification	Location of bleed/ Symptoms
NN7415-4311/ [redacted]071/ No PPX (arm 1)	3[redacted]/ HBwI	06APR20:06:50:00/ 14APR20:20:00:00	Main before trial restart	111/ 9	SPONTANEOUS/ MILD/MODERATE	LEFT ANKLE JOINT/ PAIN, SWELLING, WARM
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 4)	4[redacted]/ HBwI	28NOV20:08:00:00/ 01DEC20:08:00:00	Main after trial restart	356/ 4	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ PAIN, SWELLING, WARM, LOSS OF MOVEMENT
		19MAR21:17:00:00/ 19MAR21:23:00:00	Main after trial restart	467/ 1	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ WARM, LOSS OF MOVEMENT
		27MAY21:16:00:00/ 28MAY21:06:00:00	Extension	536/ 2	TRAUMATIC/ MILD/MODERATE	LEFT KNEE JOINT/ PAIN, SWELLING
		23JUL21:12:00:00/ 26JUL21:06:00:00	Extension	593/ 4	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ PAIN, SWELLING, WARM, LOSS OF MOVEMENT
NN7415-4311/ [redacted]072/ Concizumab PPX (arm 3)	4[redacted]/ HBwI	12APR21:06:30:00/ 13APR21:14:00:00	Main after trial restart	503/ 2	SPONTANEOUS/ MILD/MODERATE	LEFT LEG MUSCLE/ PAIN
		27AUG21:06:30:00/ 28AUG21:06:00:00	Extension	640/ 2	SPONTANEOUS/ MILD/MODERATE	RIGHT ANKLE JOINT/ PAIN, SWELLING
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 4)	1[redacted]/ HBwI	22NOV19:07:00:00/ 27NOV19:21:00:00	Main before trial restart	10/ 6	TRAUMATIC/ SEVERE	BUTTOCKS MUSCLE/ PAIN, SWELLING, WARM
		01DEC19:10:01:00/ 06DEC19:18:30:00	Main before trial restart	19/ 6	SPONTANEOUS/ MILD/MODERATE	BUTTOCKS MUSCLE/ PAIN, SWELLING, WARM, LOSS OF MOVEMENT
		10FEB20:04:00:00/ 14FEB20:03:00:00	Main before trial restart	90/ 5	SPONTANEOUS/ MILD/MODERATE	LEFT HAND MUSCLE/ PAIN, TINGLING SENSATION, WARM

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors
OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens.
CB: combined bleed.

Bleeding episodes - Japanese subjects - listing - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

Trial/ Subject ID/ Arm	Age (years)/ Haemophilia type	Onset/ Resolution	Period	Study day/ Duration (days)	Cause of bleed/ Classification	Location of bleed/ Symptoms
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 4)	1[redacted]/ HBwI	19FEB20:07:00:00/ 02MAR20:09:56:00	Main before trial restart	99/ 13	SPONTANEOUS/ MILD/MODERATE	RIGHT ARM MUSCLE/ PAIN, SWELLING, LOSS OF MOVEMENT
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 4)	1[redacted]/ HBwI	03FEB21:11:46:00/ 09FEB21:17:00:00	Main after trial restart	454/ 7	TRAUMATIC/ MILD/MODERATE	LEFT FINGERS JOINT/ PAIN, SWELLING, LOSS OF MOVEMENT
		17MAR21:07:00:00/ 18MAR21:07:00:00	Main after trial restart	496/ 2	TRAUMATIC/ MILD/MODERATE	RIGHT HIP JOINT/ PAIN
		17JUN21:13:30:00/ 26JUN21:08:55:00	Extension	588/ 10	TRAUMATIC/ MILD/MODERATE	RIGHT FINGERS JOINT/ PAIN, SWELLING
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 2)	3[redacted]/ HBwI	28OCT20:07:00:00/ 30OCT20:08:00:00	Main after trial restart	358/ 3	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ PAIN, LOSS OF MOVEMENT
		07DEC20:07:00:00/ 08DEC20:12:00:00	Main after trial restart	398/ 2	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER
		13DEC20:09:00:00/ 16DEC20:12:00:00	Main after trial restart	404/ 4	SPONTANEOUS/ MILD/MODERATE	RIGHT ELBOW JOINT/ PAIN, LOSS OF MOVEMENT
		17FEB21:07:00:00/ 21FEB21:16:00:00	Main after trial restart	470/ 5	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER
		08MAR21:07:00:00/ 10MAR21:15:00:00	Main after trial restart	489/ 3	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER
		09MAR21:02:00:00/ 15MAR21:08:00:00	Main after trial restart	490/ 7	SPONTANEOUS/ MILD/MODERATE	LEFT ELBOW JOINT/ PAIN, TINGLING SENSATION, LOSS OF MOVEMENT
		19MAR21:18:30:00/ 20MAR21:07:00:00	Main after trial restart	500/ 2	SPONTANEOUS/ MILD/MODERATE	LEFT ELBOW JOINT/ NOT REPORTED
		07APR21:17:30:00/ 08APR21:15:00:00	Main after trial restart	519/ 2	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors
OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens.
CB: combined bleed.

Bleeding episodes - Japanese subjects - listing - HAwI+HBwI - OTwoATexIR - full analysis set - trial 4311

Trial/ Subject ID/ Arm	Age (years)/ Haemophilia type	Onset/ Resolution	Period	Study day/ Duration (days)	Cause of bleed/ Classification	Location of bleed/ Symptoms
NN7415-4311/ [redacted]071/ Concizumab PPX (arm 2)	3[redacted]/ HBwI	17APR21:14:30:00/ 28APR21:11:00:00	Main after trial restart	529/ 12	SPONTANEOUS/ SEVERE	URINARY SYSTEM/ BLOOD IN URINE
		14MAY21:12:00:00/ 15MAY21:15:00:00	Main after trial restart	556/ 2	SPONTANEOUS/ MILD/MODERATE	RIGHT KNEE JOINT(CB)/ LOSS OF MOVEMENT, OTHER
		14MAY21:12:00:00/ 15MAY21:15:00:00	Main after trial restart	556/ 2	SPONTANEOUS/ MILD/MODERATE	STOMACH(CB)/ OTHER
		26MAY21:09:00:00/ 27MAY21:20:00:00	Main after trial restart	568/ 2	SPONTANEOUS/ MILD/MODERATE	RIGHT KNEE JOINT/ PAIN, LOSS OF MOVEMENT
		03JUN21:15:00:00/ 04JUN21:15:00:00	Extension	576/ 2	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER
		12JUL21:12:30:00/ 14JUL21:07:00:00	Extension	615/ 3	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ LOSS OF MOVEMENT, OTHER
		20JUL21:19:00:00/ 23JUL21:07:00:00	Extension	623/ 4	SPONTANEOUS/ MILD/MODERATE	RIGHT ELBOW JOINT/ PAIN, LOSS OF MOVEMENT
		26AUG21:12:00:00/ 29AUG21:17:00:00	Extension	660/ 4	SPONTANEOUS/ MILD/MODERATE	STOMACH/ OTHER
		30AUG21:07:00:00/ 01SEP21:07:00:00	Extension	664/ 3	SPONTANEOUS/ MILD/MODERATE	LEFT KNEE JOINT/ PAIN, LOSS OF MOVEMENT
		11OCT21:07:00:00/ 16OCT21:15:00:00	Extension	706/ 6	SPONTANEOUS/ MILD/MODERATE	LEFT HIP JOINT/ PAIN, TINGLING SENSATION, LOSS OF MOVEMENT
		04NOV21:09:10:00/ 07NOV21:17:00:00	Extension	730/ 4	SPONTANEOUS/ MILD/MODERATE	RIGHT ANKLE JOINT/ PAIN, LOSS OF MOVEMENT

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors
OTwoATexIR: On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens.
CB: combined bleed.

124 SF-36v2 (standard version) - bodily pain - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
Complete case sensitivity analysis			
N contributing to analysis	5		14
Mean score estimate at week 24	44.5		50.1
95% CI	[34.77,54.31]		[44.63,55.66]
Mean CfB score estimate at week 24	5.0		10.6
95% CI	[-4.78,14.76]		[5.08,16.12]
Difference estimate at week 24		5.61	
95% CI		[-6.10,17.32]	
p-value		0.328	
Best-worst case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	40.0		51.6
95% CI	[35.24,44.71]		[47.93,55.21]
Mean CfB score estimate at week 24	-1.8		9.8
95% CI	[-6.53,2.94]		[6.16,13.44]
Difference estimate at week 24		11.60	
95% CI		[4.96,18.23]	
p-value		<.001	
Worst-best case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	45.7		48.4
95% CI	[40.37,51.02]		[44.13,52.73]
Mean CfB score estimate at week 24	4.1		6.8

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

SF-36v2 (standard version) - bodily pain - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
95% CI	[-1.22,9.42]		[2.53,11.14]
Difference estimate at week 24		2.74	
95% CI		[-4.13,9.60]	
p-value		0.427	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

125 SF-36v2 (standard version) - physical functioning - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
Complete case sensitivity analysis			
N contributing to analysis	5		14
Mean score estimate at week 24	36.6		40.6
95% CI	[28.73,44.45]		[35.91,45.19]
Mean CfB score estimate at week 24	-1.5		2.5
95% CI	[-9.37,6.35]		[-2.19,7.09]
Difference estimate at week 24		3.96	
95% CI		[-5.25,13.18]	
p-value		0.378	
Best-worst case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	33.2		43.7
95% CI	[28.00,38.35]		[39.58,47.77]
Mean CfB score estimate at week 24	-3.8		6.7
95% CI	[-8.97,1.38]		[2.61,10.80]
Difference estimate at week 24		10.51	
95% CI		[3.57,17.44]	
p-value		0.004	
Worst-best case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	39.9		41.8
95% CI	[33.87,45.94]		[36.98,46.57]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

SF-36v2 (standard version) - physical functioning - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
Mean CfB score estimate at week 24	0.9		2.8
95% CI	[-5.09,6.98]		[-1.98,7.61]
Difference estimate at week 24		1.87	
95% CI		[-6.16,9.91]	
p-value		0.642	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

126 SF-36v2 (standard version) - mental health component score - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	19		33
N in FAS and ADS	19		29
Complete case sensitivity analysis			
N contributing to analysis	5		14
Mean score estimate at week 24	42.2		53.0
95% CI	[36.20,48.28]		[49.45,56.51]
Mean CfB score estimate at week 24	-5.4		5.3
95% CI	[-11.45,0.63]		[1.81,8.86]
Difference estimate at week 24		10.74	
95% CI		[3.62,17.87]	
p-value		0.005	
Best-worst case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	41.3		52.2
95% CI	[35.56,47.01]		[47.77,56.62]
Mean CfB score estimate at week 24	-4.2		6.7
95% CI	[-9.90,1.54]		[2.30,11.16]
Difference estimate at week 24		10.91	
95% CI		[2.96,18.86]	
p-value		0.008	
Worst-best case sensitivity analysis			
N contributing to analysis	19		29
Mean score estimate at week 24	50.2		47.0
95% CI	[45.36,55.00]		[43.09,50.87]

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit. In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

SF-36v2 (standard version) - mental health component score - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
Mean CfB score estimate at week 24	4.8		1.6
95% CI	[-0.05,9.59]		[-2.32,5.46]
Difference estimate at week 24		-3.20	
95% CI		[-9.42,3.02]	
p-value		0.306	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Complete case analysis: Change from baseline value were analysed using a mixed model for repeated measurements (MMRM), similarly to the key secondary endpoints but only based on patients with a complete set of data (Baseline, Visit 4, Visit 8, Visit 16 and Visit 24).
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.

127 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Total score - >= 17 years - week 24 - additional sensitivity analysis - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (arm 1)		Concizumab PPX (arm 2)
N in FAS	13		17
N in FAS and ADS	13		15
Best-worst case sensitivity analysis			
N contributing to analysis	13		15
Mean score estimate at week 24	68.9		26.5
95% CI	[59.98,77.82]		[18.31,34.74]
Mean CfB score estimate at week 24	16.5		-25.9
95% CI	[7.54,25.38]		[-34.13,-17.70]
Difference estimate at week 24		-42.38	
95% CI		[-55.40,-29.35]	
p-value		<.001	
Worst-best case sensitivity analysis			
N contributing to analysis	13		15
Mean score estimate at week 24	38.2		41.8
95% CI	[28.04,48.43]		[32.36,51.23]
Mean CfB score estimate at week 24	-10.6		-7.1
95% CI	[-20.83,-0.43]		[-16.51,2.37]
Difference estimate at week 24		3.56	
95% CI		[-10.88,18.00]	
p-value		0.617	

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set, CfB: change from baseline, CI: Confidence interval.
P-values are for two-sided tests of no difference from 0.
Best-worst case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 minimum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 maximum value at that visit.
Worst-best case analysis: In arm 2, patients with missing data at a certain visit were imputed as arm 2 maximum value at that visit.
In arm 1, patients with missing data at a certain visit were imputed as arm 1 minimum value at that visit.

128 SF-36v2 (standard version) - bodily pain, physical functioning and mental health component score - number of patients per visit - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX (Arm 1) N	Concizumab PPX (Arm 2) N
N in FAS	19	33
N in FAS and ADS	19	29
Bodily pain		
Baseline	10	24
Week 4	9	14
Week 8	7	19
Week 16	5	21
Week 24	7	21
Physical functioning		
Baseline	10	24
Week 4	9	14
Week 8	7	19
Week 16	5	21
Week 24	7	21
Mental health component score		
Baseline	10	24
Week 4	9	14
Week 8	7	19
Week 16	5	21
Week 24	7	21

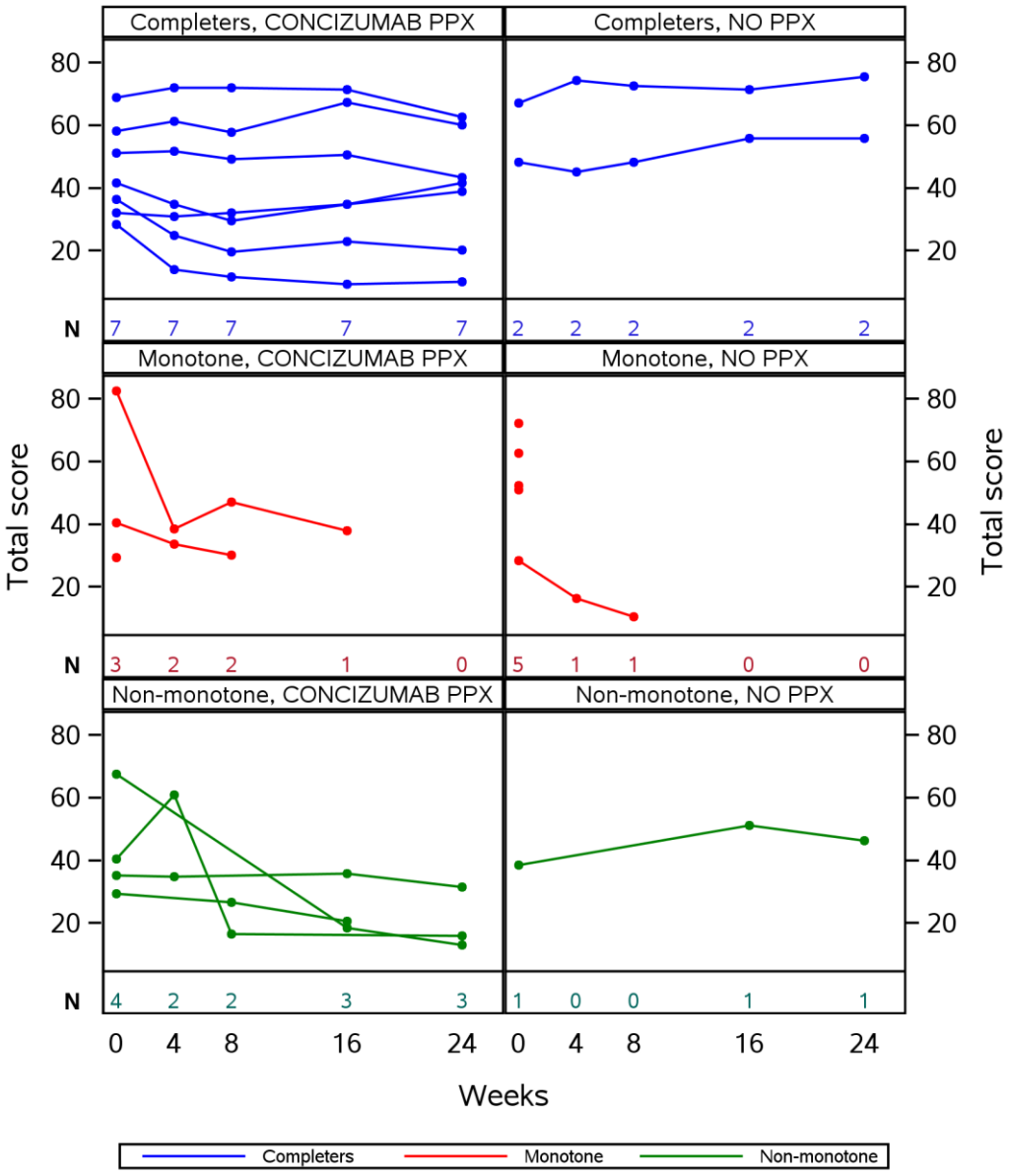
HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
The number of subjects at each visit only include subjects that have a baseline value.

129 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Total score - >= 17 years - number of patients per visit - HAwI+HBwI - OTexIR - full analysis set - trial 4311

	No PPX	Concizumab PPX
	(Arm 1) N	(Arm 2) N
N in FAS	13	17
N in FAS and ADS	13	15
Total score		
Baseline	8	14
Week 4	3	11
Week 8	3	11
Week 16	3	11
Week 24	3	10

HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis, N: number of subjects, FAS: Full analysis set, ADS: Analysis data set.
The number of subjects at each visit only include subjects that have a baseline value.
Three subjects <17 years old filled out the questionnaire. These data are included in the descriptive statistics, though not counted in 'N in FAS' and 'N in FAS and ADS'.

130 Haemophilia quality of life questionnaire for adults (Haem-A-QoL) - Total score - >= 17 years - spaghetti plot - HAwI+HBwI - OTexIR - full analysis set - trial 4311



HAwI: haemophilia A with inhibitors, HBwI: haemophilia B with inhibitors, OTexIR: On-treatment without data on initial regimen, PPX: Prophylaxis.
Post baseline data is only displayed for subjects with a baseline.
Three subjects <17 years old filled out the questionnaire. These data are included.
Week 0 includes baseline records collected at visit 1/1a and visit 2/2a.

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