

Supplemental materials

Figure S1. ABRs for BAY 81-8973 administered two times weekly versus rAHF-PFM (Valentino)

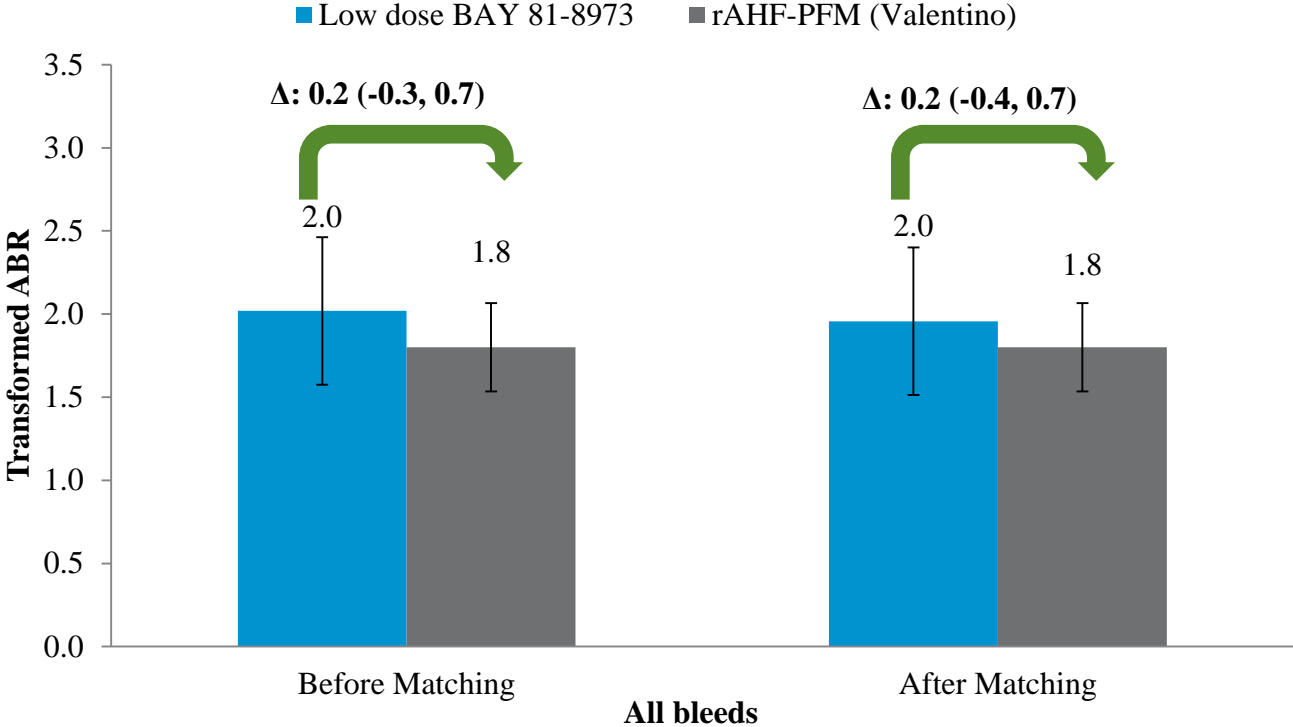


Figure S2. ABRs for BAY 81-8973 administered two times weekly versus rAHF-PFM (Tarantino)

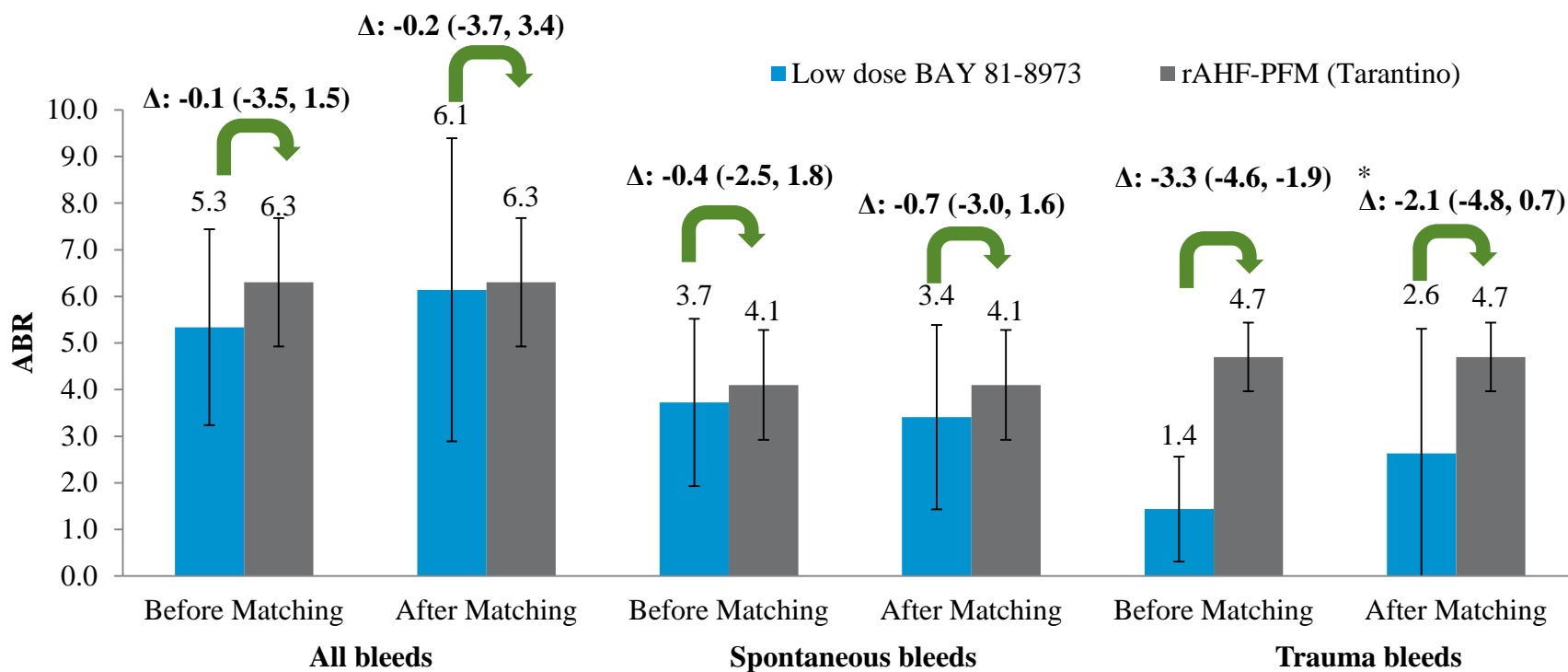


Figure S3. ABRs for BAY 81-8973 administered two times weekly versus turoctocog alfa

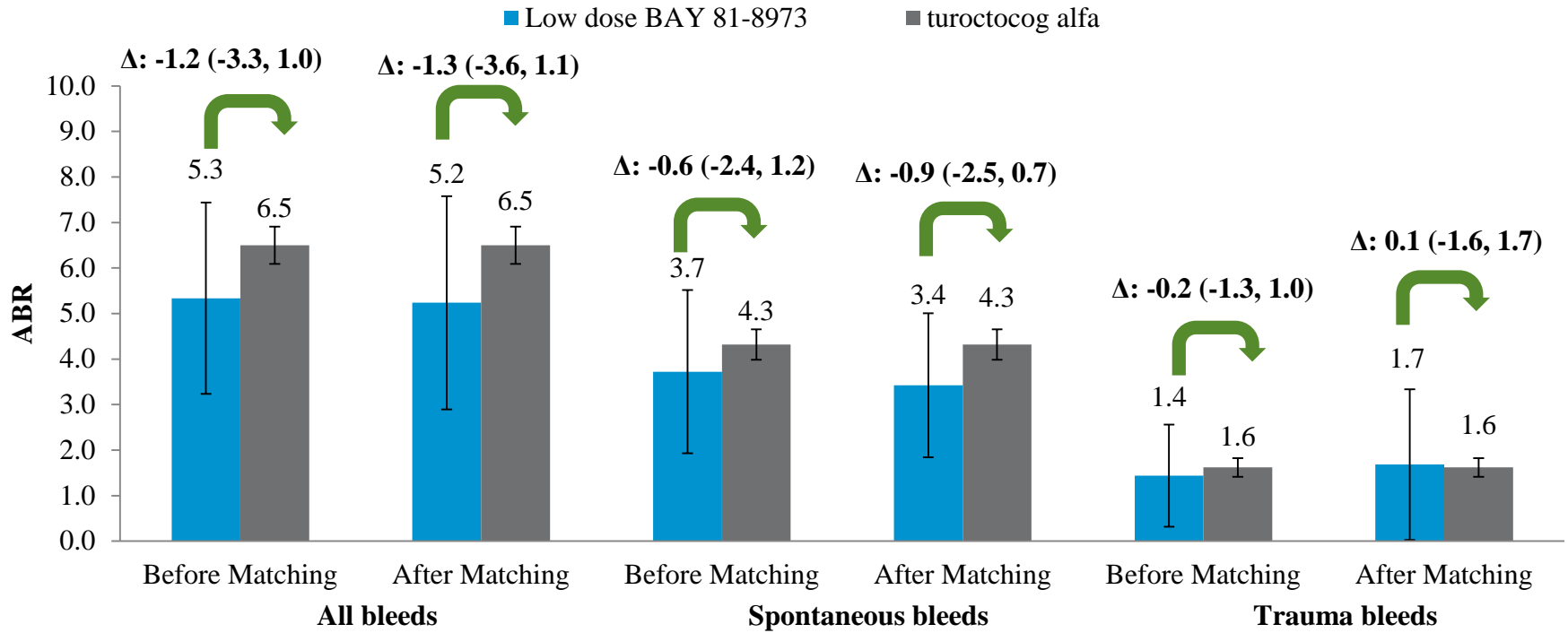


Table S1. Inclusion and exclusion criteria for screening

Inclusion Criteria	Exclusion Criteria
Language	
<ul style="list-style-type: none"> • Studies in English 	<ul style="list-style-type: none"> • Studies not in English
Study design and publication type	
<ul style="list-style-type: none"> • Randomized controlled trials (RCTs) • Single-arm trials 	<ul style="list-style-type: none"> • Reviews (SLR and narrative reviews)* • Observational studies • Case reports • Commentaries and letters • Recommendations/guidelines
Study population	
<ul style="list-style-type: none"> • Adult and adolescent patient with severe hemophilia A 	<ul style="list-style-type: none"> • Non-human studies • Studies focusing on pediatric patients • Not hemophilia A • Not severe hemophilia A patients**
Study interventions	
<ul style="list-style-type: none"> • rAHF-PFM • turoctocog alfa 	<ul style="list-style-type: none"> • Studies that do not include rAHF-PFM or turoctocog alfa

Notes:

* Reviews were flagged and excluded. References were checked for potential articles.

** Studies with mixed severe and moderately severe hemophilia A patients may be included.

Table S2. Outcomes for BAY 81-8973 administered two times weekly (first six-month) versus rAHF-PFM (Tarantino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 46)		(N = 107)			(N = 46)		(N = 107)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	33%		30%		3%	33%		30%		3%
ABR, mean (SD)										
All bleeds	6.8	(8.7)	6.3	(8.7)	0.5	7.3	(9.4)	6.3	(8.7)	1.0
Spontaneous bleeds	4.9	(8.2)	4.1	(8.2)	0.8	4.3	(7.6)	4.1	(8.2)	0.2
Trauma bleeds	1.5	(4.3)	4.7	(4.3)	-3.2*	2.8	(6.5)	4.7	(4.3)	-1.9

Table S3. Outcomes for BAY 81-8973 administered two times weekly (first six-month) versus turoctocog alfa

	Before matching					After matching				
	BAY 81-8973		turoctocog alfa		Difference	BAY 81-8973		turoctocog alfa		Difference
	(N = 46)		(N = 150)			(N = 46)		(N = 150)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	33%		30%		3%	28%		30%		-2%
ABR, mean (SD)										
All bleeds	6.8	(8.7)	6.5	(2.5)	0.3	6.5	(8.3)	6.5	(2.5)	0.0
Spontaneous bleeds	4.9	(8.2)	4.3	(2.1)	0.6	4.5	(7.1)	4.3	(2.1)	0.2
Trauma bleeds	1.5	(4.3)	1.6	(1.3)	-0.1	1.8	(5.1)	1.6	(1.3)	0.2

Table S4. Outcomes for BAY 81-8973 in LEOPOLD II versus rAHF-PFM (Valentino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 59)		(N = 66)			(N = 59)		(N = 66)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	27%		33%		-6%	27%		33%		-6%
Transformed ABR, mean (SD)										
All bleeds	2.0	(1.3)	1.8	(1.1)	0.2	2.0	(1.3)	1.8	(1.1)	0.2

Table S5. Outcomes for BAY 81-8973 in LEOPOLD II versus rAHF-PFM (Tarantino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 59)		(N = 107)			(N = 59)		(N = 107)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	27%		30%		-3%	28%		30%		-2%
ABR, mean (SD)										
All bleeds	4.9	(6.8)	6.3	(6.8)	-1.4	5.0	(6.9)	6.3	(6.8)	-1.3
Spontaneous bleeds	3.5	(6.0)	4.1	(6.0)	-0.6	3.5	(6.0)	4.1	(6.0)	-0.6
Trauma bleeds	1.3	(2.3)	4.7	(2.3)	-3.4*	1.5	(2.4)	4.7	(2.3)	-3.2*

Table S6. Outcomes for BAY 81-8973 in LEOPOLD II versus turoctocog alfa

	Before matching					After matching				
	BAY 81-8973		turoctocog alfa		Difference	BAY 81-8973		turoctocog alfa		Difference
	(N = 59)		(N = 150)			(N = 59)		(N = 150)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	27%		30%		-3%	26%		30%		-4%
ABR, mean (SD)										
All bleeds	4.9	(6.8)	6.5	(2.5)	-1.6	4.3	(6.6)	6.5	(2.5)	-2.2
Spontaneous bleeds	3.5	(6.0)	4.3	(2.1)	-0.8	3.1	(6.0)	4.3	(2.1)	-1.2
Trauma bleeds	1.3	(2.3)	1.6	(1.3)	-0.4	1.1	(2.1)	1.6	(1.3)	-0.6

Table S7. Outcomes for BAY 81-8973 (first six-month) in LEOPOLD II versus rAHF-PFM (Tarantino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 28)		(N = 107)			(N = 28)		(N = 107)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	32%	30%	2%	39%	30%	9%				
ABR, mean (SD)										
All bleeds	6.0	(8.3)	6.3	(8.3)	-0.3	6.1	(8.5)	6.3	(8.3)	-0.2
Spontaneous bleeds	4.3	(7.6)	4.1	(7.6)	0.2	4.2	(7.6)	4.1	(7.6)	0.1
Trauma bleeds	1.4	(3.3)	4.7	(3.3)	-3.3*	1.8	(3.5)	4.7	(3.3)	-2.9*

Table S8. Outcomes for BAY 81-8973 (first six-month) in LEOPOLD II versus turoctocog alfa

	Before matching					After matching				
	BAY 81-8973		turoctocog alfa		Difference	BAY 81-8973		turoctocog alfa		Difference
	(N = 59)		(N = 150)			(N = 59)		(N = 150)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	32%		30%		2%	31%		30%		1%
ABR, mean (SD)										
All bleeds	6.0	(8.3)	6.5	(2.5)	-0.5	5.3	(8.0)	6.5	(2.5)	-1.2
Spontaneous bleeds	4.3	(7.6)	4.3	(2.1)	-0.1	3.9	(7.4)	4.3	(2.1)	-0.4
Trauma bleeds	1.4	(3.3)	1.6	(1.3)	-0.2	1.2	(2.8)	1.6	(1.3)	-0.5

Table S9. Outcomes for BAY 81-8973 administered two times weekly in LEOPOLD II versus rAHF-PFM (Valentino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 28)		(N = 66)			(N = 28)		(N = 66)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	29%		33%		-5%	37%		33%		4%
Transformed ABR, mean (SD)										
All bleeds	2.1	(1.3)	1.8	(1.1)	0.3	2.0	(1.4)	1.8	(1.1)	0.2

Table S10. Outcomes for BAY 81-8973 administered two times weekly in LEOPOLD II versus rAHF-PFM (Tarantino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 28)		(N = 107)			(N = 28)		(N = 107)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	29%	30%	-1%	40%	30%	10%				
ABR, mean (SD)										
All bleeds	5.7	(7.2)	6.3	(7.2)	-0.6	5.7	(7.7)	6.3	(7.2)	-0.6
Spontaneous bleeds	4.5	(7.1)	4.1	(7.1)	0.4	4.6	(7.5)	4.1	(7.1)	0.5
Trauma bleeds	0.9	(1.5)	4.7	(1.5)	-3.8*	1.0	(1.6)	4.7	(1.5)	-3.7*

Table S11. Outcomes for BAY 81-8973 administered two times weekly in LEOPOLD II versus turoctocog alfa

	Before matching					After matching				
	BAY 81-8973		turoctocog alfa		Difference	BAY 81-8973		turoctocog alfa		Difference
	(N = 28)		(N = 150)			(N = 28)		(N = 150)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	29%	30%	-1%	33%	30%	3%				
ABR, mean (SD)										
All bleeds	5.7	(7.2)	6.5	(2.5)	-0.8	4.5	(6.6)	6.5	(2.5)	-2.0
Spontaneous bleeds	4.5	(7.1)	4.3	(2.1)	0.2	3.4	(6.3)	4.3	(2.1)	-0.9
Trauma bleeds	0.9	(1.5)	1.6	(1.3)	-0.7*	0.9	(1.7)	1.6	(1.3)	-0.7

Table S12. Outcomes for BAY 81-8973 administered two times weekly (first six-month) in LEOPOLD II versus rAHF-PFM (Tarantino)

	Before matching					After matching				
	BAY 81-8973		rAHF-PFM		Difference	BAY 81-8973		rAHF-PFM		Difference
	(N = 28)		(N = 107)			(N = 28)		(N = 107)		
	[A]	[B]	[A - B]	[C]	[D]	[C - D]				
Patients with zero bleeds, %	29%	30%	-1%	40%	30%	10%				
ABR, mean (SD)										
All bleeds	7.6	(9.1)	6.3	(9.1)	1.3	7.6	(9.6)	6.3	(9.1)	1.3
Spontaneous bleeds	6.2	(9.3)	4.1	(9.3)	2.1	6.2	(9.5)	4.1	(9.3)	2.1
Trauma bleeds	1.0	(1.7)	4.7	(1.7)	-3.7*	1.2	(1.7)	4.7	(1.7)	-3.5*

Table S13. Outcomes for BAY 81-8973 administered two times weekly (first six-month) in LEOPOLD II versus turoctocog alfa

	Before matching					After matching				
	BAY 81-8973		turoctocog alfa		Difference	BAY 81-8973		turoctocog alfa		Difference
	(N = 28)		(N = 150)			(N = 28)		(N = 150)		
	[A]		[B]		[A - B]	[C]		[D]		[C - D]
Patients with zero bleeds, %	29%		30%		-1%	33%		30%		3%
ABR, mean (SD)										
All bleeds	7.6	(9.1)	6.5	(2.5)	1.1	6.0	(8.3)	6.5	(2.5)	-0.5
Spontaneous bleeds	6.2	(9.3)	4.3	(2.1)	1.9	4.8	(8.1)	4.3	(2.1)	0.5
Trauma bleeds	1.0	(1.7)	1.6	(1.3)	-0.6	1.0	(1.8)	1.6	(1.3)	-0.6