April 28, 2022

The supply of plasma-derived medicinal products in the future of Europe

28-29 April 2022 – Rome, Italy

in collaboration with FIODS

Coagulation Factors

Professor Bülent ZULFIKAR, MD

SESSION 2 - CLINICAL USE AND FUTURE TRENDS

Chairpersons: P.M. MANNUCCI, L. DE MARCO

14:00	Polyvalent immunoglobulins - I. QUINTI
14:25	Albumin - S. D. RYDER
14:50	Factor VIII and other coagulation factors - O. B. ZÜLFIKAR
15:15	Alpha-1-Proteinase Inhibitor - S. SCARLATA
15:40	C1-Esterase Inhibitors – M. CANCIAN

Prof. Dr. Bülent Zülfikar – Istanbul University

	DECLARATION – CONFLICT OF INTEREST
Research Supports	*Pfizer, Sobi, Novo Nordisk*
Company (ies) Worked for	*NONE*
Equity Partnership	*NONE*
Consulting / Donation Review Committee	*Takeda, Pfizer, Novo Nordisk, Sobi, Bayer, Sanofi, BioMarin*
Scientific Consulting	*Roche, Sobi, Novo Nordisk*

Goals and Objectives

- To give an overview of all pipeline options
- To set up for the talks of the future days
  (on patient choices, preferences, new centre structures/care pathways)
- To offer a patient and local perspective on how to compare options
  (not how to choose between them)

Coagulopathy - Inherited Bleeding Disorders

- **von Willebrand Disorders (vWD)**
- **Hemophilia A / B and Hemophilia Carriers**
- **Rare Bleeding Disorders** (RBD)
  - Fibrinogen (Factor I), F II, V, VII, X, XI, XIII,
  - Combined factor deficiencies
- Platelet Function Disorders (PFD)
  - Glanzmann's Thrombasthenia
  - Bernard Soulier Syndrome
  - Others
- Other
  - Hereditary Hemorrhagic Telangiectasia
  - Ehlers Danlos Syndrome

Hereditary Bleeding Disorders and Treatment Centers

Country	Population – million	PwH + vWD + RBD	Registered	HTC*
USA	328,5	18.008 + 12.394 + 4.809	35.211	146
UK	67	8.397 + 11.066 + 10.258	29.721	87
Germany	83	4.523 + 4.505 + ?	9.037+	60
France	67	8.330 + 2.742 + 1.120	12.192	36
Turkey**	82	5.738 + 1.119 + 2.290	9.147*	15
Nederlands	17,5	1.277 + 346 + 82	1.705	11
Belgium	19	1.267 + 2.106 + 535	3.908	10
Sweden	15	972 + 286 + ?	1.258+	3

*: Hemophilia Treatment Center
**: Turkish data from hemophiLINE 2015

WFH Annual Global Survey – 2019.

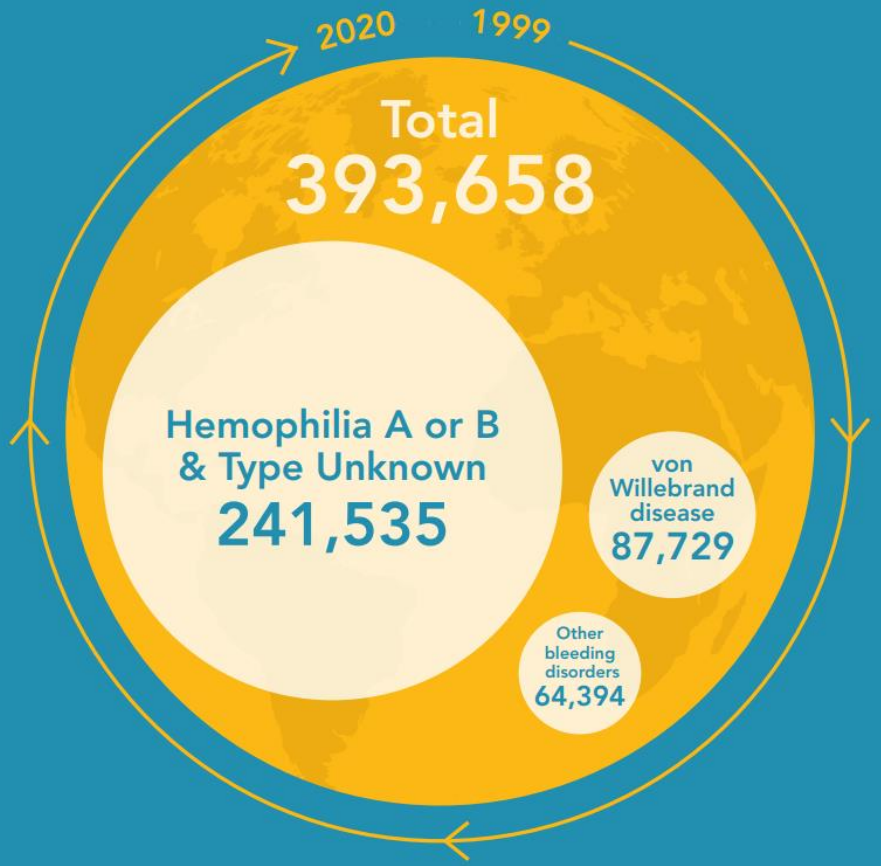
REPORT ON THE ANNUAL GLOBAL SURVEY 2020 SUMMARY DEMOGRAPHICS

TABLE 2. **Demographics**

	2020 Total
Number of countries in this survey	**120**
World population covered by countries in this survey report	**5,728,473,350**
Total number of people with bleeding disorders	**347,026**
Number of people with Hemophilia	**209,614**
Number of people with hemophilia A	**165,379**
Number of people with hemophilia B	**33,076**
Number of people with hemophilia type unknown or type not reported	**11,159**
Number of people with VWD	**84,197**
Number of people with Other Bleeding Disorders	**53,215**

GLOBAL REPRESENTATION OVER TIME (1999–2020)

Since 1999, there have been 144 different countries that have reported data to the Annual Global Survey. This infographic contains historical data from the Annual Global Survey. That is, if a country reported data one year and not the next, the older data were used under the assumption that the number of patients did not change substantially from one year to the next. This section was added to illustrate a more complete representation of the current state of patient identification globally.



Bleding Disorders in Turkiye (HemophiLINE 2015)

	Hemophilia A & B		RFD ve PFD	vWH	Population
	4.860	878			
n. %	5.738 (62,8)		2.290 (25)	1119 (12,2)	80.336.904

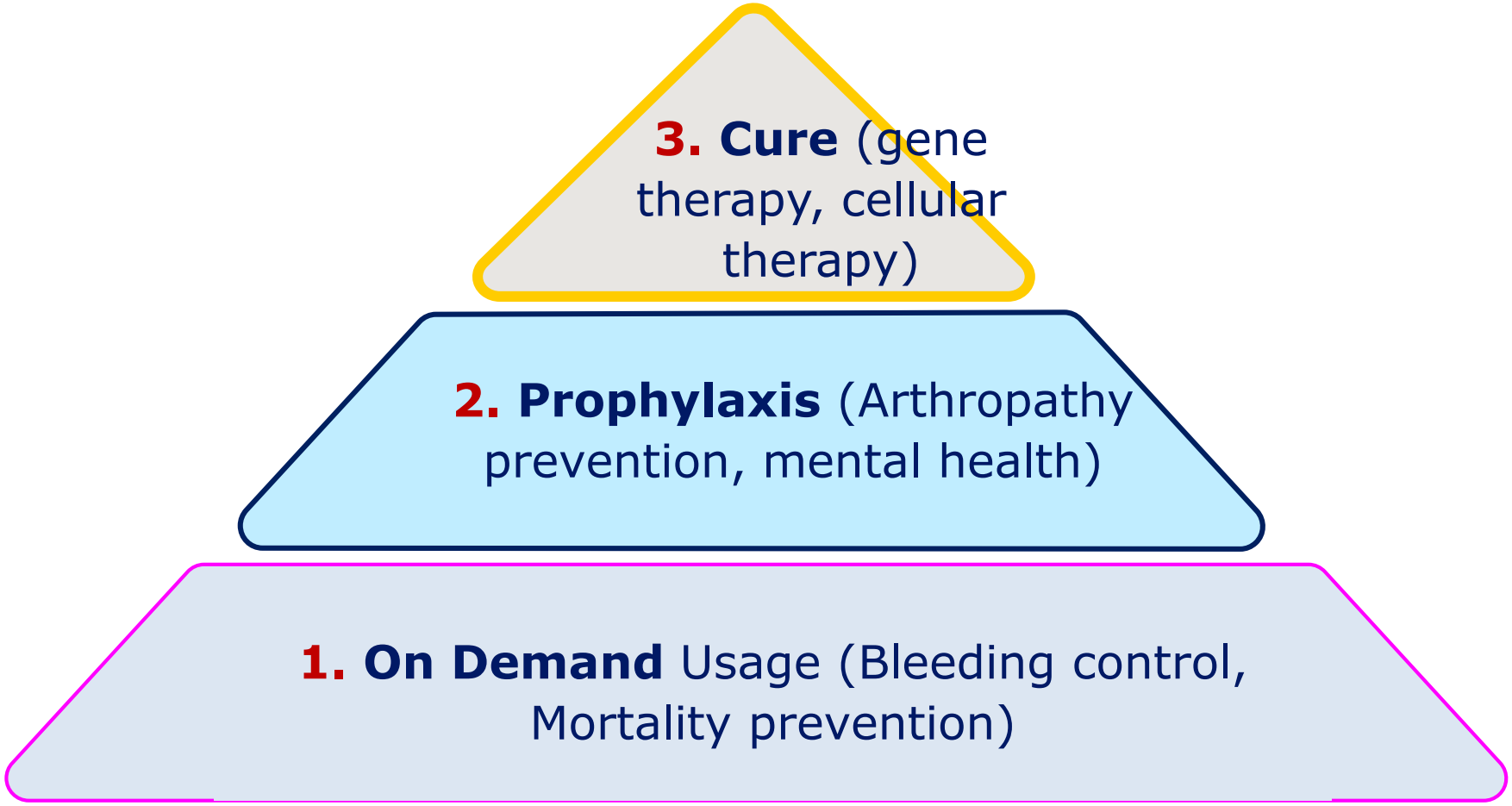
Factors which should be considered in Herdeitary Bleeding Disorders Care

- Long-term well-being
- Higher plasma level
- Bleeding frequency reduction (Zero Bleed)
- Joint health
- Ability to be active and functional
- Normal Q of L

- School attendence
- Have a job /career
- Have a family /social life
- Be active /sports
- Not feeling the burden of the disease

1.Nugent D, Kalnins W, Querol F, et al. Haemophilia 2015; 21:e26–e38.2. Krishnan S, Haemophilia. 2015;21:64–70.

3 Stages in Coagulation Disorders



Standart Guidelines – for Diagnosis, Treatment, and Follow up

Indian Pediatr. 2018 Jul 15;

Consensus Stat
Hemophilia.

Sachdeva A[1], Gunasekar
Management

Collabor
Author in

1 Sir Gan Marrow
2 Sir Gan
3 All Indi
4 Army H
5 Sawai M
6 Indrapr
7 Rainbo
8 St John

Zhonghua X

[Consensus of

[Article in Chinese]

Thrombosis and Hemost

PMID: 28565732 DOI: 10

[Indexed for MEDLINE]

WFH Guidelines for the Managemer
Hemophilia, 3rd Edition

[Treatment of haemophilia in Austria].

[Article in German]
Pabinger I[1], Heistinger M[2], Muntean W[3], Reitter-Pfoertner SE[4], Rosenlechner S[5], Schindl T[6], Sch

Author information

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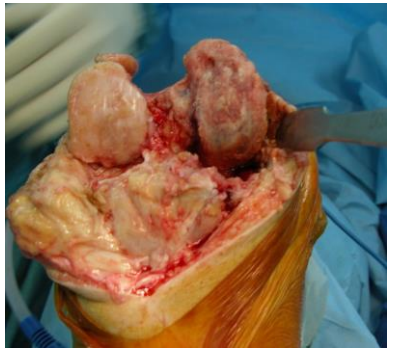
8 Department für Kinder- und Jugendheilkunde, Medizinische Universität Innsbruck, In
9 Universitätsklinik für Kinder- und Jugendheilkunde, Medizinische Universität Wien, V

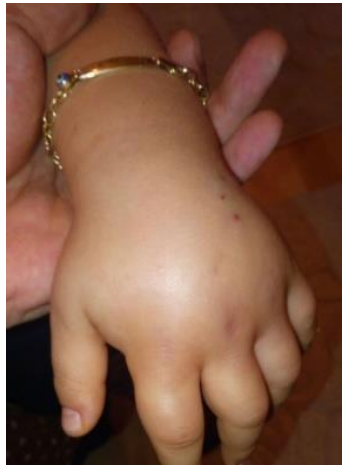
Abstract

This guideline which is endorsed by the Austrian Society of Haemophilia, the Austrian Haematology & Medical Oncology is intended to give a clear and practical guidance for diagnosing and treating treatment of haemophilia there are few controlled interventional trials, and recommendations usually have a rat

Replacement Therapy



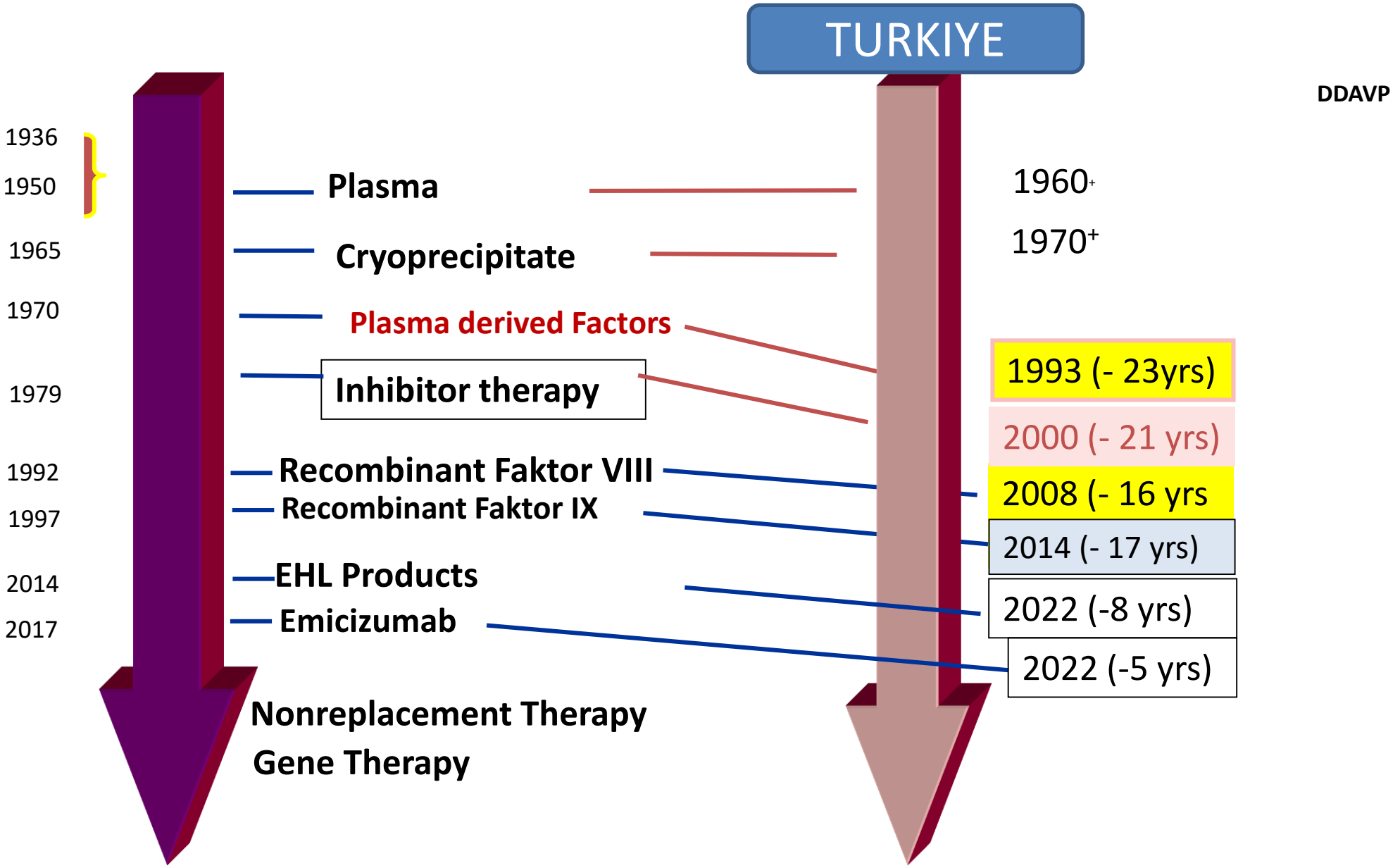
- RT has been the cornerstone of the management of Hereditary Bleeding Disorders
  - to reduce mortality
  - to reduce morbidity of chronic crippling arthropathy.
- However, RT is associated with a risk for inhibitor development
  - adversely affects bleeding prevention
  - adversely affects outcomes.



- Frequent intravenous injections are burdensome and costly,
  - with poor adherence
  - with restricted access

Mancuso ME et al. The changing treatment landscape in haemophilia: Lancet 2021; 397: 630

HISTORY OF TREATMENT OPTIONS



FVIII in Hemophilia A Treatment

Plasma derived factors

(since 1970)

- Beriate
- Factane
- Fanhdi
- Immunate
- Octanate
- Emoclate
- Factor 8Y
- Haemoctin SDH
- Koate DVI

Recombinant factors

– Standart half-life (since 1992)

Kogenate FS – Refacto AF – Advate – Novoeight – Afstyla – Nuviq - Kovaltry

– Extended half-life (since 2014)

Elocta/Eloctate – Jivi – Adynovate/Adynovi – Esperoct – **BIVV001 (?)**

FVIII Mimetics - EMC (since 2017)

Half-life

Faktör VIII: ~12 hour. (prophylaxis: 2-3 dose/week)

Doses

On demand; 50 – 100 IU/kg. (prophylaxis; 25 – 40 IU/kg

Powell et al Blood 2012. Coyle et al JTH 2014. Mahlangu et al Blood 2014.
Mannucci P. Hemophilia therapy: the future has begun. Haematologica. 2020 Mar;105(3):545-553. *WFH Guidelines For The Management Of Hemophilia*

FIX in Hemophilia B Treatment

Factor IX

Plasma derived factor IX

- Aimafix
- Berinin
- Betafact
- Immunine
- Octanine
- Replenine

- Recombinant factor IX
  - Standart (BeneFix)
  - Extended half-life

    (Alprolix – Idelvion – Refixia/Rebinyn – Rixubis)
    (**DalcA**-delcinonacog alfa – phase2)

NFRP in clinical trial

- Anti TFPI
  - Concizumab
  - Marstacimab
- Anti AT
  - Fitusiran

Half-life

Factor IX: 24 hour. 256 hour (prophylaxis: 1-2/w. – 1 in every 2w)

Doses

On demand; 60-100, 60-80 IU/kg Prophylaxis; 40 IU/kg

1.M. Richards, British Journal of Haematology, 149, 498–507. 2. J. Batllea. Blood Coagulation and Fibrinolysis 2008, 19:333–340.
3. E. P. Mauser-Bunschoten Haemophilia (2001), 7, 96-98 4.WFH Guidelines For The Management Of Hemophilia

Treatment for Hemophilia with Inhibitor

- Plasma derived aPCC
  - FEIBA

- Recombinant factor VII
  - NovoSeven
  - Aryoseven
  - Sevenfact
  - Marzeptocog alfa (SC, Phase 3)

Half-life

FEIBA: 8-12 hour. NovoSeven: 2-3 hour. Sevenfact: 2-3 hour (prophylaxis: 1-7/w)

Doses

FEIBA; 50 – 100 IU/kg NovoSeven; 90µg/kg Sevenfact: 75µg/kg

1.M. Richards, British Journal of Haematology, 149, 498–507. 2. J. Batllea. Blood Coagulation and Fibrinolysis 2008, 19:333–340.
3. E. P. Mauser-Bunschoten Haemophilia (2001), 7, 96-98 4.WFH Guidelines For The Management Of Hemophilia

Treatment for vWD and Rare Factor Deficiencies

Haemate-P	
Wilate	
Wilfactin	
Rec.vWF (Veyvondi)	

Hemocomplettan	Fibrinogen df
Fibrogammin	FXIII df
Cofact, Kascadil	FX, FVII, FII
Immuseven	Factor VII
Coagadex, Factor X P	Factor X
Homoeleven	Factor XI

Products for Bleeding Disorders in TURKIYE

Plasma Derived Factors

Emoclot Hemofil-M Octanate	Fandhi Haemoctin Beriate (since 1993)
Octanine Aimafix	Immunine Berinin (Faktör IX) Betafact
vWF Faktör I (Fibrinojen) Faktör XIII FII, FV, FVII, FX FXI aPCC	Haemate-P Hemocomplettan Fibrogammin Cofact - FEIBA

Recombinant Factors

Recombinate - Advate
Kogenate-FS
Refacto AF
Novoeight
Kovaltry
(since 2007)

BeneFix (Factor IX)

NovoSeven
Aryoseven (rec.FVIIa)

FVIII Mimetics

Hemlibra

Treatment of Hemophilia — More Amazing Progress

Pier M. Mannucci, M.D.

With a prevalence of 17.1 cases per 100,000 males, hemophilia A is the most frequent inherited disorder of blood coagulation.[1] After the adoption of prophylactic replacement therapy with factor VIII administered intravenously 3 or 4 times per week, patients' life expectancy has become very close to that of unaffected males.[1] Moreover, the occurrence of spontaneous bleeding and the development of musculoskeletal damage have been minimized. In addition, in the past decade, further impressive advances have occurred.[2,3] The arrival of factor VIII products with an extended plasma half-life has meant that intravenous injections that are needed to minimize bleeding can be administered twice weekly.[4] The monoclonal antibody emicizumab, which mimics factor VIII coagulant activity, is efficacious at preventing bleeding when administered subcutaneously at weekly intervals or even every 2 weeks.[5,6] Promising results from phase 1–2 studies of gene transfer with adeno-associated viral vectors[7] involving adults with severe hemophilia A paved the way to phase 3 studies in an advanced phase of development.[8]

The New England Journal of Medicine

N Eng J Med. Sept.10, 2020

ORIGINAL ARTICLE

BIVV001 Fusion Protein as Factor VIII Replacement Therapy for Hemophilia A

Barbara A. Konkle, M.D., Amy D. Shapiro, M.D., Doris V. Quon, M.D., Ph.D., Janice M. Staber, M.D., Roshni Kulkarni, M.D., Margaret V. Ragni, M.D., M.P.H., Ekta S. Chhabra, Ph.D., Stacey Poloskey, M.D., Kara Rice, M.S., Suresh Katragadda, Ph.D., Dan Rudin, M.D., Joachim Fruebis, Ph.D., and Craig C. Benson, M.D.

From Bloodworks Northwest and the University of Washington, Seattle (B.A.K.); Indiana Hemophilia and Thrombosis Center, Indianapolis (A.D.S.); the Orthopaedic Hemophilia Treatment Center, Los Angeles (D.V.Q.); the University of Iowa, Iowa City (J.M.S.); Michigan State University, East Lansing (R.K.); the Department of Medicine, University of Pittsburgh, and the Hemophilia Center of Western Pennsylvania, Pittsburgh (M.V.R.); and Sanofi (E.S.C., S.P., S.K., C.C.B.) and Bioverativ (K.R., D.R., J.F.) — both in Waltham, MA. Address reprint requests to Dr. Konkle at Bloodworks Northwest, 921 Terry Ave., Seattle, WA 98104, or at barbarak@bloodworksnw.org.

This article was updated on March 11, 2021, at NEJM.org.

N Engl J Med 2020;383:1018-27.
DOI: 10.1056/NEJMoa2002699

ABSTRACT

BACKGROUND

Factor VIII replacement products have improved the care of patients with hemophilia A, but the short half-life of these products affects the patients' quality of life. The half-life of recombinant factor VIII ranges from 15 to 19 hours because of the von Willebrand factor chaperone effect. BIVV001 (rFVIIIFc-VWF-XTEN) is a novel fusion protein designed to overcome this half-life ceiling and maintain high sustained factor VIII activity levels. Data are lacking on the safety and pharmacokinetics of single-dose BIVV001.

METHODS

In this phase 1–2a open-label trial, we consecutively assigned 16 previously treated men (18 to 65 years of age) with severe hemophilia A (factor VIII activity, <1%) to receive a single intravenous injection of recombinant factor VIII at a dose of 25 IU per kilogram of body weight (lower-dose group) or 65 IU per kilogram (higher-dose group). This injection was followed by a washout period of at least 3 days. The patients then received a single intravenous injection of BIVV001 at the same corresponding dose of either 25 IU or 65 IU per kilogram. Adverse events and pharmacokinetic measurements were assessed.

RESULTS

No inhibitors to factor VIII were detected and no hypersensitivity or anaphylaxis events were reported up to 28 days after the injection of single-dose BIVV001. The geometric mean half-life of BIVV001 was three to four times as long as that of recombinant factor VIII (37.6 hours vs. 9.1 hours in the lower-dose group and 42.5 vs. 13.2 hours in the higher-dose group); the area under the curve (AUC) for product exposure was six to seven times as great in the two dose groups (4470 hours vs. 638 hours × IU per deciliter in the lower-dose group and 12,800 hours vs. 1960 hours × IU per deciliter in the higher-dose group). After the injection of BIVV001 in the higher-dose group, the mean factor VIII level was in the normal range (≥51%) for 4 days and 17% at day 7, which suggested the possibility of a weekly interval between treatments.

CONCLUSIONS

In a small, early-phase study involving men with severe hemophilia A, a single intravenous injection of BIVV001 resulted in high sustained factor VIII activity levels, with a half-life that was up to four times the half-life associated with recombinant factor VIII, an increase that could signal a new class of factor VIII replacement therapy with a weekly treatment interval. No safety concerns were reported during the 28-day period after administration. (Funded by Sanofi and Sobi; ClinicalTrials.gov number, NCT03205163.)

KEY NUMBERS FROM THE REPORT ON THE ANNUAL GLOBAL SURVEY 2020

For all tables and graphs from this point onwards, the analyses were done using only data from countries that responded in 2020.

120 **NUMBER OF COUNTRIES** in this survey

RESPONSE RATE from WFH National Member Organizations **82%** (120/147)

347,026 **NUMBER OF IDENTIFIED PATIENTS**

- **209,614** People with hemophilia
- **165,379** Hemophilia A
- **33,076** Hemophilia B
- **11,159** Hemophilia type unknown
- **84,197** von Willebrand disease
- **53,215** Other bleeding disorders

FACTOR

FACTOR VIII USAGE PER CAPITA
0.945 IU (0.106-4.469) Median (IQR) 105 countries

FACTOR IX USAGE PER CAPITA
0.13 IU (0.015-0.662) Median (IQR) 98 countries

FACTOR USAGE SUMMARY

TABLE 3. Factor VIII usage 2020

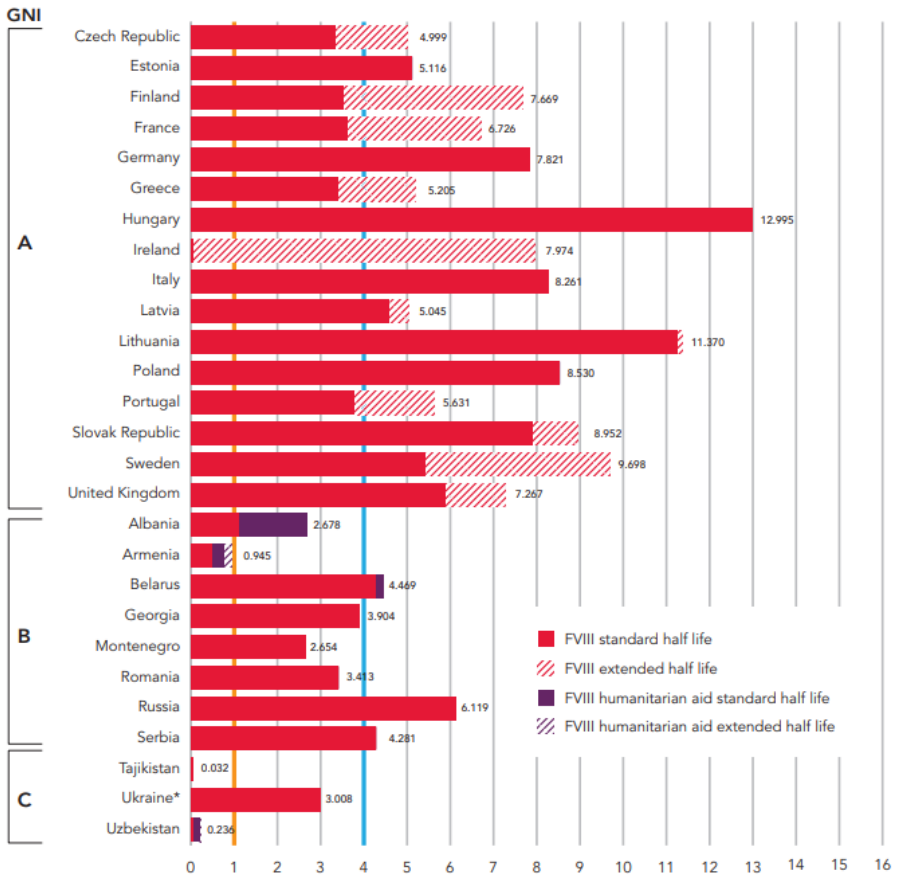
	FACTOR USAGE	NUMBER OF COUNTRIES REPORTING
Mean (SD) global per capita factor VIII usage	**2.551 IU (3.108)**	**105**
Median global per capita factor VIII usage	**0.945**	**105**
Interquartile range (IQR) global per capita factor VIII usage	**4.363 IU (0.106 to 4.469)**	**105**
Total consumption of factor VIII concentrates	**11,116,204,164 IU**	**105**

TABLE 4. Factor IX usage 2020

	FACTOR USAGE	NUMBER OF COUNTRIES REPORTING
Mean (SD) global per capita factor IX usage	**0.485 IU (0.872)**	**98**
Median global per capita factor IX usage	**0.13 IU**	**98**
Interquartile range (IQR) global per capita factor IX usage	**0.647 IU (0.015 to 0.662)**	**98**
Total consumption of factor VIII concentrates	**2,202,597,368 IU**	**98**

The average per capita and total consumption figures reported this year cannot be directly compared to the figures from other survey years as the group of countries reporting factor usage changes from year to year. To illustrate, if a large country using large amounts of factor or a large country using very little factor, reports one year and not the next, then this will have a significant effect on the mean and median from year to year. The standard deviation (SD) describes the amount of variation of dispersion from the mean. The interquartile range (IQR) describes the middle 50% of reported numbers and is less likely to be distorted by outliers (extreme values).

FIGURE G4a. **Mean per capita factor VIII use in 2020 – regional and GNI comparisons of IU/total population: Europe**

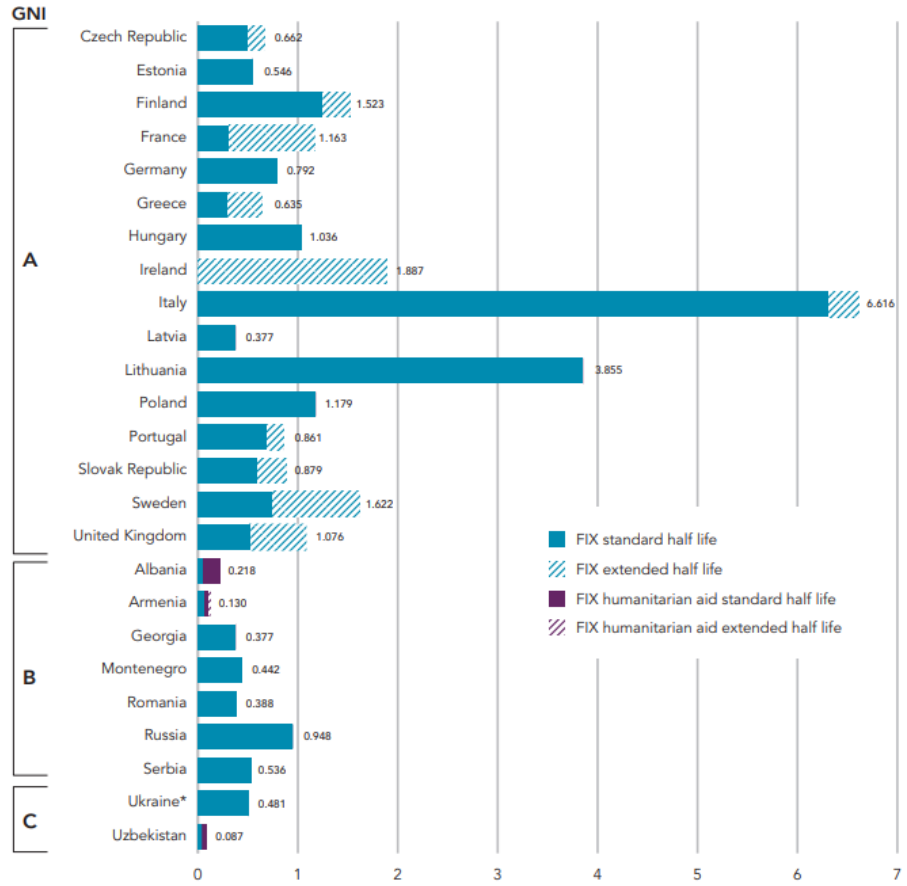


Economic category based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)". GNI in US dollars: D low income, $0–$1,045; C lower middle income, $1,046–$4,095; B upper middle income, $4,096–$12,695; and A high income, $12,695 or more.

PLEASE NOTE: The x-axis showing the number of IU/capita is different in each graph of Figure G. The orange line indicates 1 international unit (IU) per capita of factor VIII. The WFH has established that one IU of FVIII clotting factor concentrate per capita should be the target minimum for countries wishing to achieve survival for the hemophilia population. Higher levels would be required to preserve joint function or achieve a quality of life equivalent to an individual without hemophilia. The European Department for the Quality of Medicines and Healthcare (EDQM) recommends the minimum consumption of factor VIII and IX concentrate in any country should be 4 IU and 0.5 IU per capita of general population respectively. Please note the orange line does not apply to factor IX. Only countries that provided product use data in the 2020 questionnaire are included in Figure G graphs. It may be that countries used extended half-life products but did not report the amount. These will be shown as part of the standard half-life products.

** Data updated after publication. These updates are not reflected in any other calculations or summary tables in this report.*

FIGURE G4b. **Mean per capita factor IX use in 2020 – regional and GNI comparisons of IU/total population: Europe**



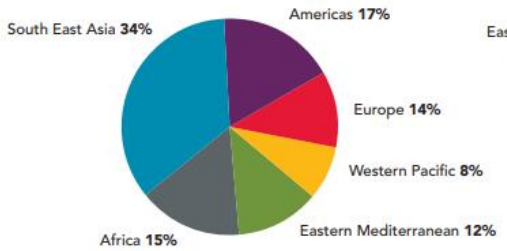
Economic category based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)". GNI in US dollars: D low income, $0–$1,045; C lower middle income, $1,046–$4,095; B upper middle income, $4,096–$12,695; and A high income, $12,695 or more.

PLEASE NOTE: The x-axis showing the number of IU/capita is different in each graph of Figure G. Only countries that provided product use data in the 2020 questionnaire are included in Figure G graphs. It may be that countries used extended half-life products but did not report the amount. These will be shown as part of the standard half-life products. The European Department for the Quality of Medicines and Healthcare (EDQM) recommends the minimum consumption of factor VIII and IX concentrate in any country should be 4 IU and 0.5 IU per capita of general population respectively.

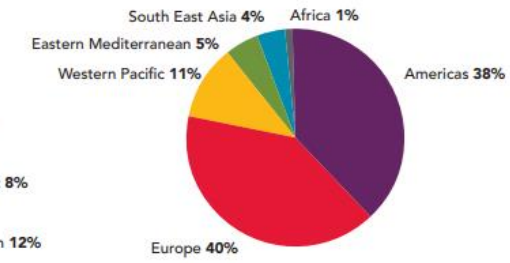
** Data updated after publication. These updates are not reflected in any other calculations or summary tables in this report.*

FIGURE D. **Global distribution of factor VIII use**

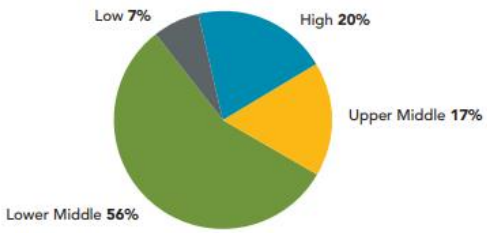
Population by region



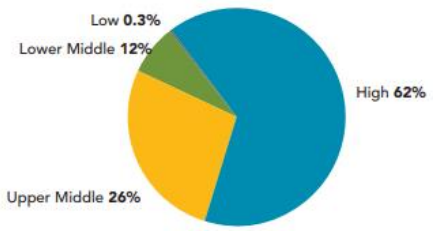
FVIII total IU by region



Population by gross national income



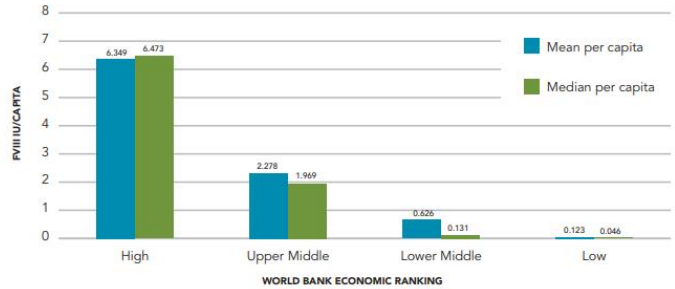
Total FVIII IU by gross national income



Economic category based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)". GNI in US dollars: D low income, $0–$1,045; C lower middle income, $1,046–$4,095; B upper middle income, $4,096–$12,695; and A high income, $12,695 or more.

FIGURE E. **Mean and median global factor VIII per capita 2020**

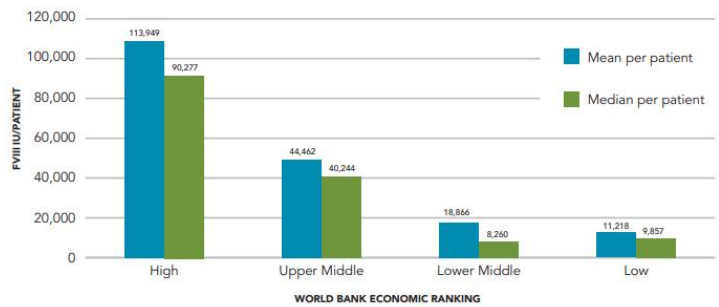
(Data from 101 countries.)



Economic category based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)". GNI in US dollars: D low income, $0–$1,045; C lower middle income, $1,046–$4,095; B upper middle income, $4,096–$12,695; and A high income, $12,695 or more.

FIGURE F. **Mean and median global factor FVIII per patient 2020**

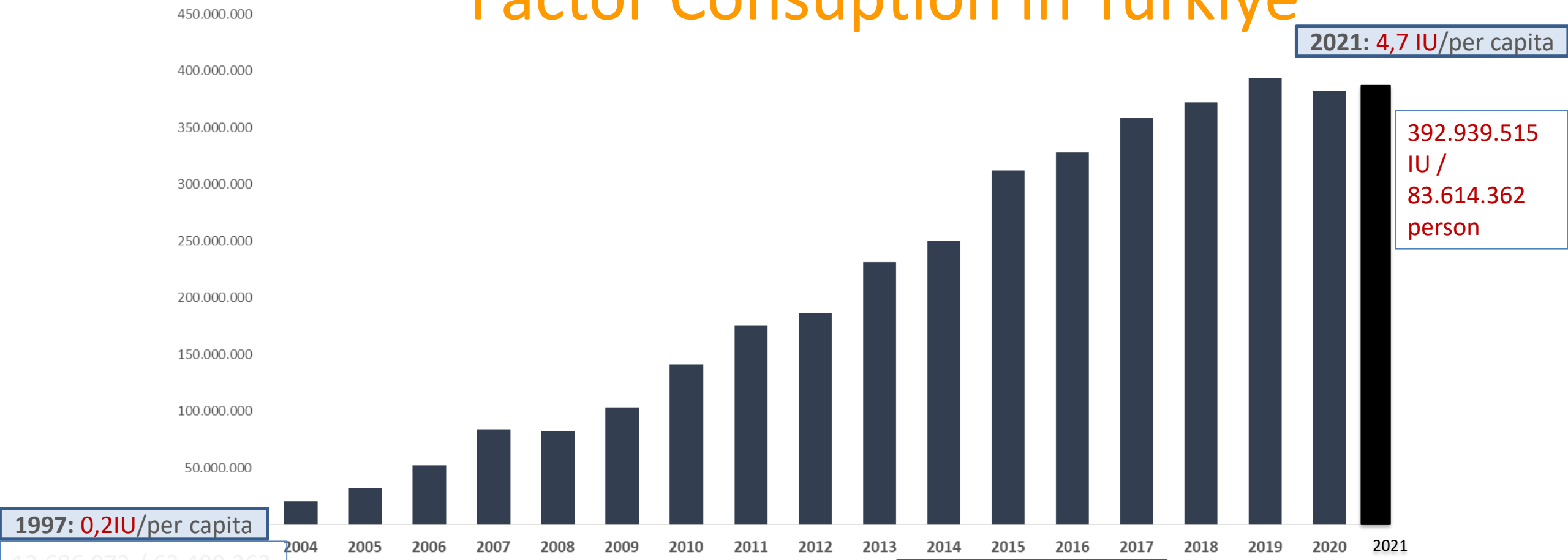
(Data from 101 countries.)



Economic category based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)". GNI in US dollars: D low income, $0–$1,045; C lower middle income, $1,046–$4,095; B upper middle income, $4,096–$12,695; and A high income, $12,695 or more.

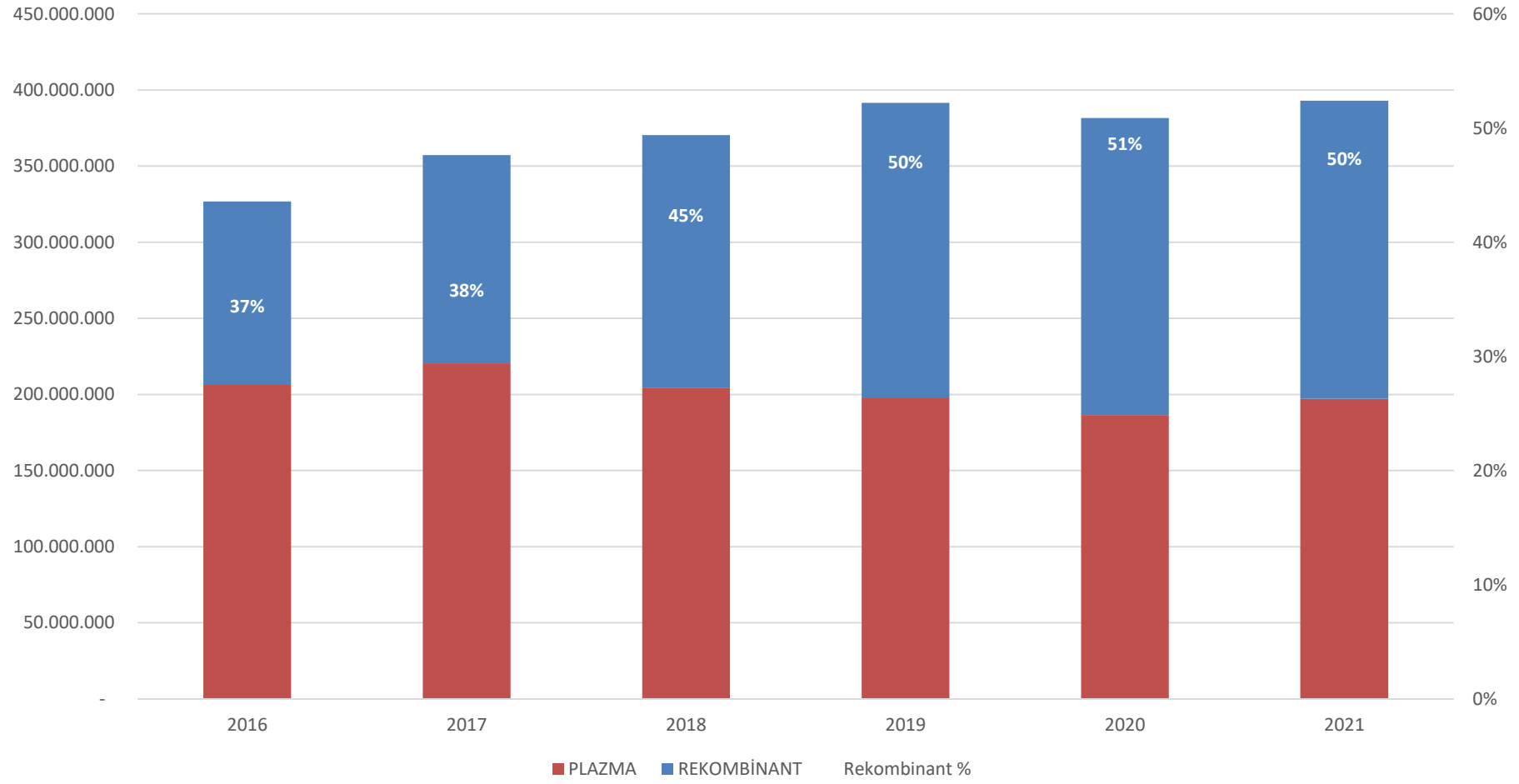
Numbers in Figure F are calculated based on reported factor VIII use and the number of identified hemophilia A patients. We do not have data on individual treatment. WFH humanitarian aid donations are included.

Factor Consuption in Turkiye



(HemophiLINE, 2015)

Factor Consuption in Turkiye



	2016	2017	2018	2019	2020	2021
REKOMBİNANT	120,540,000	136,833,500	165,972,750	193,975,750	195,005,250	195,797,152
Plasma derived	206,232,500	220,483,500	204,479,500	197,572,500	186,553,500	197,142,364
TOTAL	326,772,500	357,317,000	370,452,250	391,548,250	381,558,750	392,939,515
Rekombinant %	37%	38%	45%	50%	51%	50%

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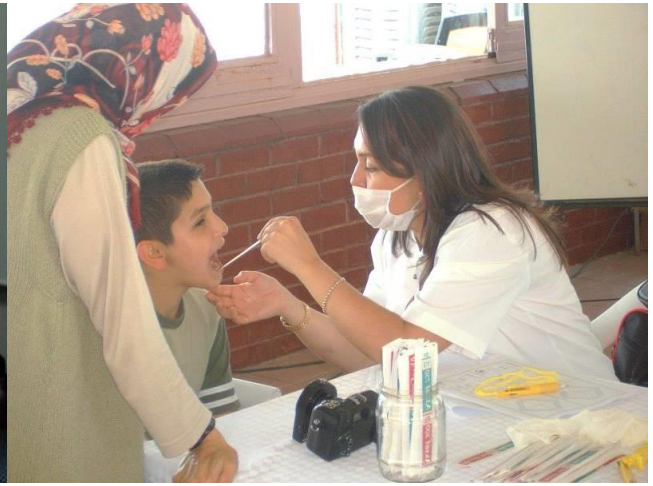
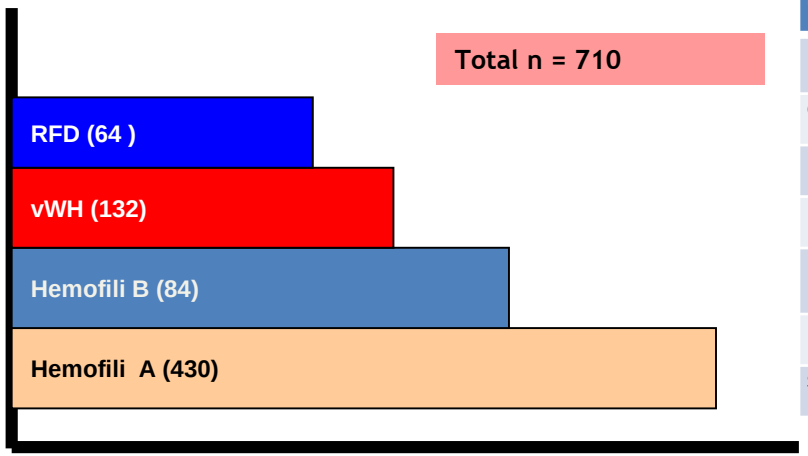
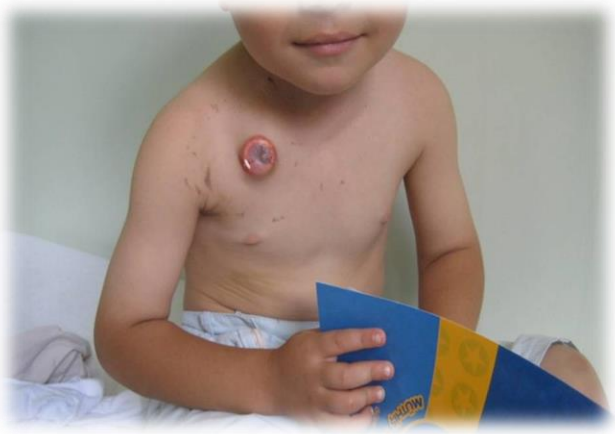


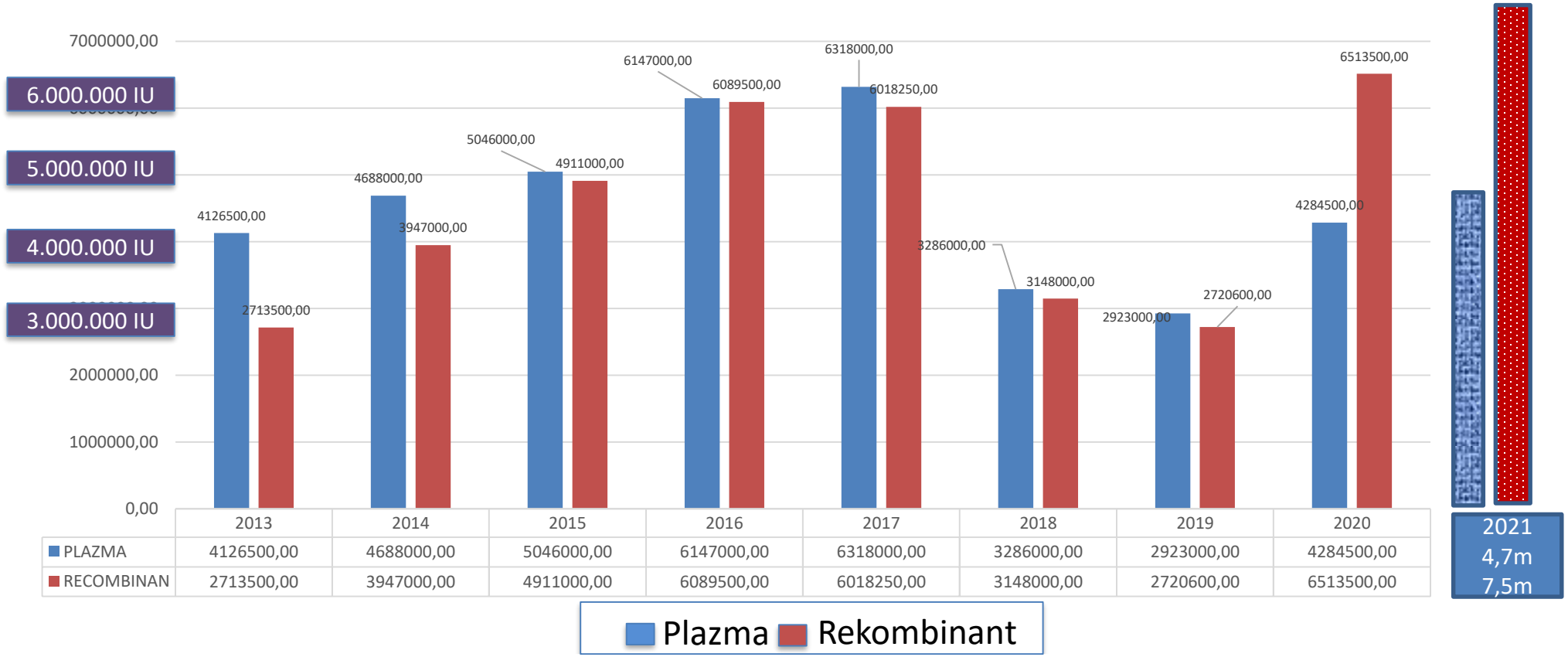


Multidisipliner Ekip	
Hematoloji	2+2
Ortopedi	2+2
Diş Hekimi	1+2
Nükleer Tıp	1+1
Fizyoterapi	1+1
Hemşire	2
Sekreter / Veri giriş elemanı	2

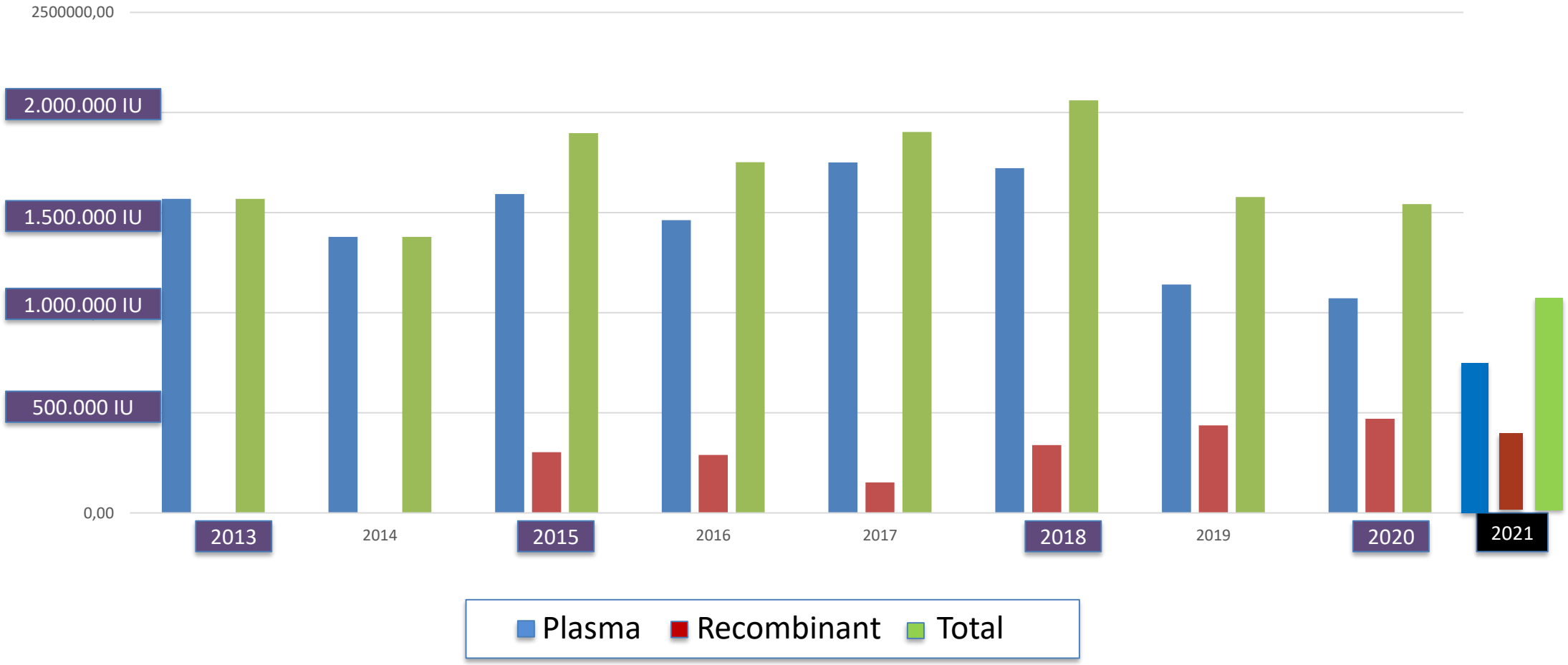


FVIIIs

Hastalık	n
Hemofili A	430
Hemofili B	84
vWB	132
NFE	64
Toplam	710



FIXs


2500000,00
2.000.000 IU
1.500.000 IU
1.000.000 IU
500.000 IU
0,00
2013
2014
2015
2016
2017
2018
2019
2020
2021
Plasma
Recombinant
Total

	2013	2014	2015	2016	2017	2018	2019	2020
Inhibitor								
FEIBA	541.000	1.181.000	1.618.000	2.103.500	1.248.500	529.000	88.500	908.500
NovoSeven	1248	2469	2269	1748	1930	1083	1522	4736

COMPLIANCE

Prophylaxis - 2-3 times a week do you do it regularly?

Original Article

Persons With Hemophilia of Generation Y and Their Relatives Attitudes and Expectations From Treatment

Bulent Zulfikar, MD[1,2], Basak Koc, MD[1], Irmak Gumustas, MD[2], and Haluk Zulfikar, MA, MSc, Phd[3]

Clinical and Applied Thrombosis/Hemostasis
Volume 27: 1-6
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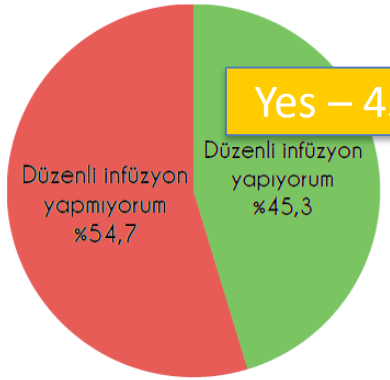
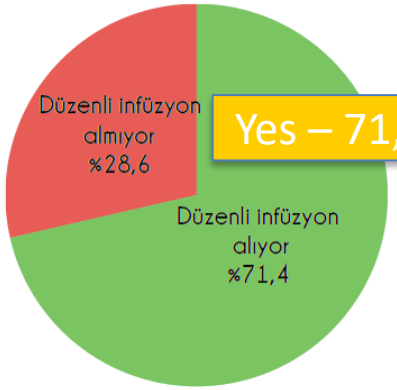
PwHs * (n: 64)



Yes – 45,3%

Relatives **(n: 56)



Yes – 71,4%

Tablo 24: Hastanın Tedavisine Uyumu Artıran Etkenler İçin İlişki Analizi Sonuçları

		Hemofilik		Hemofilik Birey Yakını		Ki Kare Testi	
		Sayı	Yüzde	Sayı	Yüzde	X^2	p
Ne olsaydı tedaviye uyumunuz artardı?	Damar yolunun daha kolay bulunmasını ve acıyı hafifletecek yöntemlerin bulunması	2	3,3	10	19,2		
	İlaca erişim kolaylığının olması	16	26,7	4	7,7		
	Özel tedavi desteği ve hemofili tedavi merkezlerinin kurulması	17	28,3	24	46,2	18,276	0,001*
	Daha etkili yeni ilaçların geliştirilmesi	9	15,0	2	3,8		
	Diğer	16	26,7	12	23,1		

*p<0,05: İlişki Var

Araştırma sonuçlarına göre hemofilik hastalar ile hasta yakınlarının, hastanın tedavisine uyumunu artıracak faktörlere ilişkin görüşleri arasında istatistiksel olarak önemli farklılık

MENTAL HEALTH

TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2014) 44: 1087-1090
© TÜBİTAK
doi:10.3906/sag-1310-82

An examination of the symptoms of anxiety and parental attitude in children with hemophilia

Osman ABALI[1], Osman Bülent ZÜLFİKAR[2,3], Sevcan KARAKOÇ DEMİRKAYA[1], Hamza AYAYDIN[1], Fuat KIRCELLİ[1], Mehtap DUMAN[3]

[1]Department of Child and Adolescent Psychiatry, İstanbul Faculty of Medicine, İstanbul University, İstanbul, Turkey
[2]Department of Pediatric Hematology- Oncology, Cerrahpaşa Faculty of Medicine, İstanbul University, İstanbul, Turkey
[3]The Hemophilia Society of Turkey, İstanbul,

Received: 22.10.2013 • **Accepted:** 28.12.2013 • **Published Online**

Background/aim: Hemophilia is an inherited disease with serious repercussions. Psyc and adolescents with hemophilia. The aim of this study was to assess symptoms of a attitude towards children with hemophilia.

Materials and methods: 42 boys were assessed according to child and adolescent psy were obtained by the State-Trait Anxiety Scale, the Self-Report for Childhood Anxie Attitude Research Instrument (PARI).

Results: The mean age was 11.6 ± 2.5 (range; 7–16). State anxiety scores (44.02 ± 6.9) The most interesting results were high scores related to overprotective mothering (47 (39.4 ± 9.1). The total SCARED scores obtained were (23.25 ± 11.3).

Conclusion: Assuring a high quality of life is important for children and adolescents affected by psychiatric symptoms (e.g. anxiety symptoms, depression, intra-familial This study suggests that high anxiety scores and problems related to parental attituc hemophilia. These problems caused by parental attitude and anxiety symptoms should

Key words: hemophilia, child, psychiatry, family, psychology

Haemophilia
The Official Journal of the World Federation of Hemophilia,
European Association for Haemophilia and Allied Disorders and
the Hemostasis & Thrombosis Research Society

Haemophilia (2016), **22**, e25–e29
DOI: 10.1111/hae.12801

ORIGINAL ARTICLE *Musculoskeletal*

Benefits of radial head excision in patients with haemophilia: mid-term functional results

A.C. ATALAR,* B. KOC,† F. BIRISIK,* A. ERSEN* and B. ZULFİKAR†
**Department Of Orthopaedics and Traumatology, Istanbul Medical Faculty, Istanbul University, Fatih; and †Department Of Pediatric Haemotology and Oncology, Cerrahpasa Medical Faculty and Oncology Institute, Istanbul University, Cerrahpasa, Istanbul, Turkey*

Introduction: Recurrent haemarthrosis in haemophilic patients result with arthropathy of the radiocapitellar joint and blockage of the forearm rotation. **Aim:** The aim of this study is to evaluate the mid-term results of radial head excision with partial synovectomy in severe haemophilic patients retrospectively. **Methods:** Persistent pain and decreased forearm rotation were the main indications for radial head excision. Between 2002 and 2013, radial head excisions were performed for 14 elbows of 14 patients. Eleven patients were haemophilia A, whereas two patients were haemophilia B patients and the remaining one had von Willebrand (Type 3) disease. The mean age of the patients was 29 at the time of the surgery. The mean follow-up was 51 (12–155) months. VAS (visual analogue score) for pain, forearm rotation, qDASH and MEPS (Mayo Elbow Performance Score) were used as the primary outcome parameters. **Results:** The mean VAS decreased significantly from 6.5 preoperatively to 2.2 at the final follow-up ($P = 0.0003$). The mean forearm rotation increased from 40° to 115° respectively ($P = 0.0007$). In two patients, efficacious rotation increase was not achieved due to distal radioulnar joint problems. The mean qDASH score and MEPS were 18.1 and 87.5 at the latest follow-up, respectively, where four patients had excellent and 10 patients had good results. **Conclusions:** Radial head excision is a safe and effective procedure for haemophiliac patients with radiocapitellar arthropathy and decreased forearm rotation. Distal radioulnar joint should be evaluated preoperatively which may impair the results.

Keywords: elbow arthropathy, haemophilia, radial head excision

SURGERY

Haemophilia
The Official Journal of the World Federation of Hemophilia,
European Association for Haemophilia and Allied Disorders and
the Hemostasis & Thrombosis Research Society

Haemophilia (2012), 1–6
DOI: 10.1111/hae.12059

ORIGINAL ARTICLE

Long-term outcomes in haemophilic synovitis after radiosynovectomy using rhenium-186: a single-centre experience

B. ZULFIKAR,* C. TURKMEN,† O. KILICOGLU,‡ F. DIKICI,‡ F. BEZGAL,§ O. GORGUN¶ and O. TASER§
**Department of Pediatric Hematology and Oncology, Cerrahpasa Medical Faculty, Institute of Oncology, Istanbul University, clear Medicine, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey; umatology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey; bul, Turkey; and ¶Department of Pediatric Hematology and Oncology, Institute of ul, Turkey*

is been performed
ars in our hospital.
erm outcome in the
TP) analysis and the
g radiosynovectomy
emophilic synovitis.
n 165 joints (81
nd 2 hip joints) of
8.0 ± 7.5 years; 91
ia B and 2 von
ne 2001 and July
48 months (range: 9
aled that patients'
iosynovectomy was
and elbow joints.
tween the ankle and
months respectively;
elationship between

the TTP and the following variables: age, type and severity of haemophilia, the presence or absence of inhibitor, the radiological score, range of motion (ROM) status of joints and the pretreatment bleeding frequency. In this study, 18–20% of the treated joints had improved ROM and 82–79% of the treated joints had unchanged ROM after treatment both the ankle and elbow joints respectively. In this report including TTP analysis in the largest series with long-term follow-up, we demonstrated long-term effectiveness of Re-186 radiosynovectomy in haemophilic synovitis. In our experience, the main predictor of outcome following radiosynovectomy is the number of joint bleeding within 6 months after therapy.

Keywords: ankle, elbow, haemophilic synovitis, radio-synovectomy, Re-186, shoulder

Conclusion

- If haemophilia and other hereditary bleeding disorders (HBD) aren’t treated, joint damage and disabilities occur due to the bleeding
- Treatments that we have for over 40 years, besides stopping bleeding, have complications (viral transmission, inhibitor formation)
- Replacement Therapy is cornerstone of the management of HBD.
- In the last 5 years; there has been great developments in the haemophilia treatment.
- However; much more care must be taken for fewer problems.

Conclusion

- Products in Clinical Trial
- Patients Needs
- Local Experience and Knowledge

It must be thoroughly synthesized and then reflected in real life

- Plasma-derived products are the mother of treatment. Pioneer. And indispensable.
- Difficulties in plasma collection increase the cost of these products.
- Advances in recombinant technology are appealing to patients.

The spread of knowledge and experience enables more physicians and more centers to become familiar with non-replacement products.

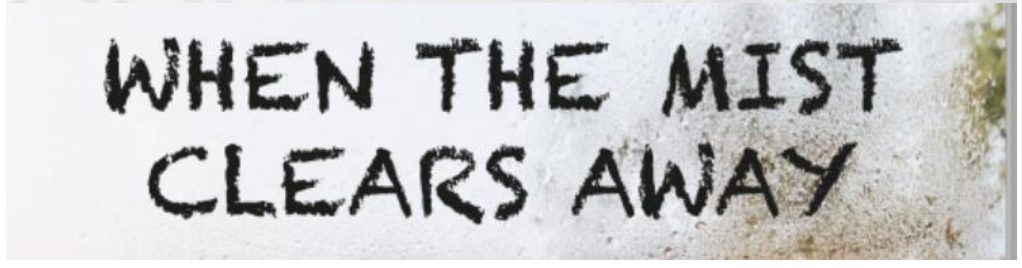
1992
TRHD
TÜRKİYE HEMOFİLİ DERNEĞİ
THE HEMOPHILIA SOCIETY OF TURKEY

2005
HEMOFİLİ FEDERASYONU
FEDERATION OF HEMOPHILIA

19th INTERNATIONAL HEMOPHILIA CONGRESS of TURKEY

17-20 November 2022

Nirvana Cosmopolitan
Lara - Antalya



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İstanbul - 1982

THANK YOU