

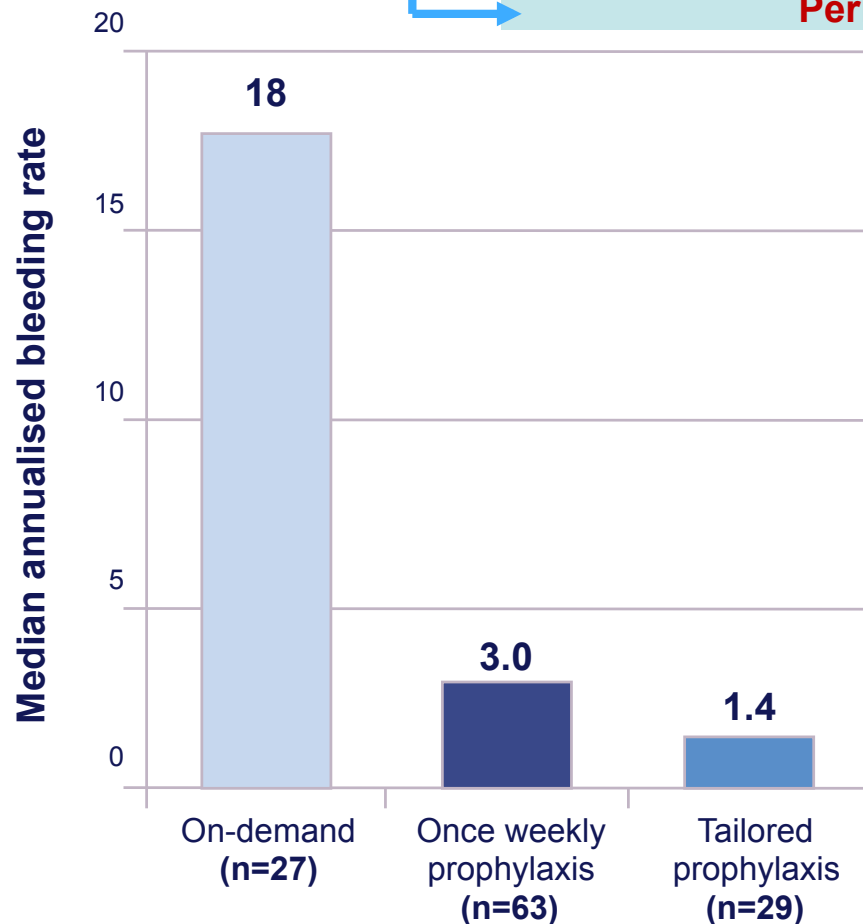
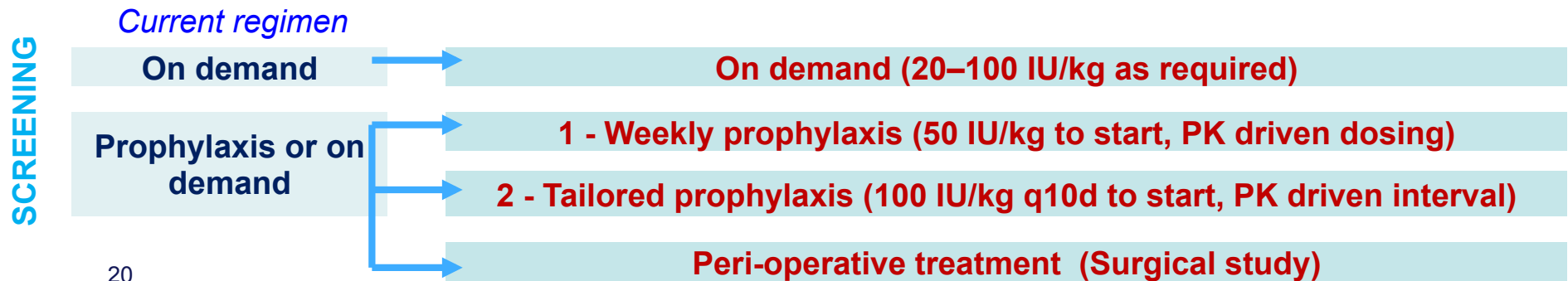
I nuovi concentrati di fattori della coagulazione a lunga emivita nel trattamento del paziente emofilico

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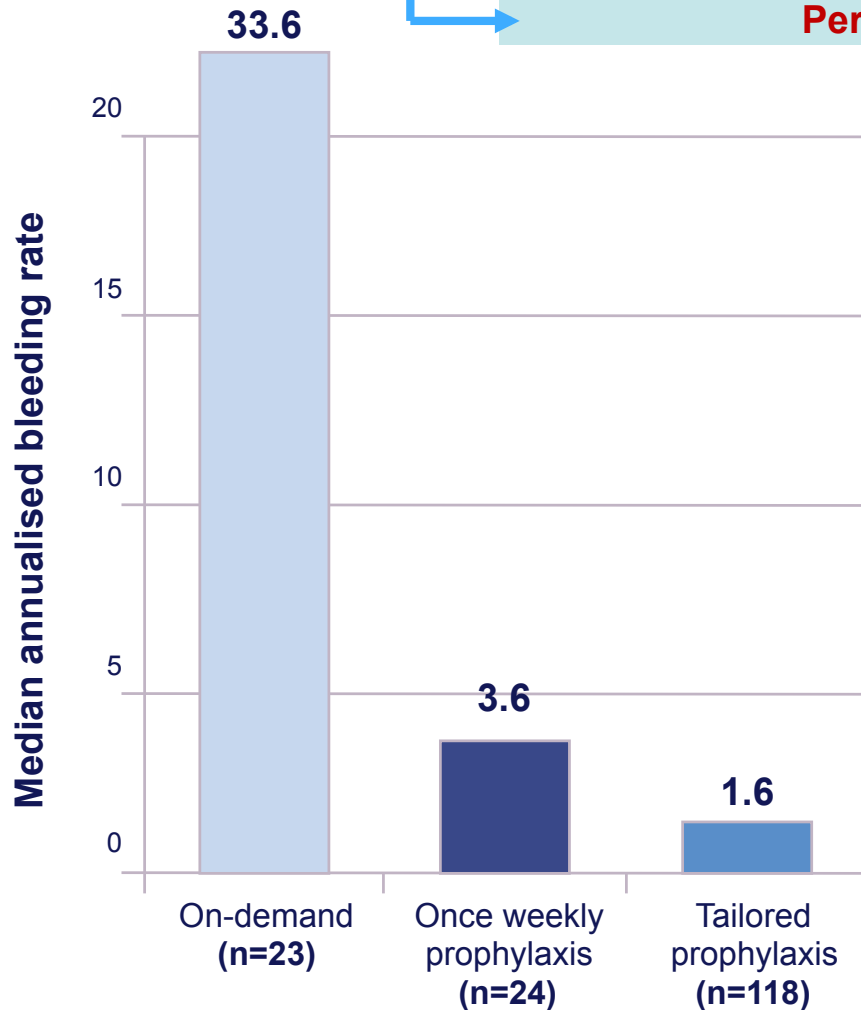
***Giornate Ematologiche Vicentine – VII edizione
Palazzo Bonin Longare, 10-12 ottobre 2016***

B-LONG: Phase 3 Study of rFIXFc in PTPs



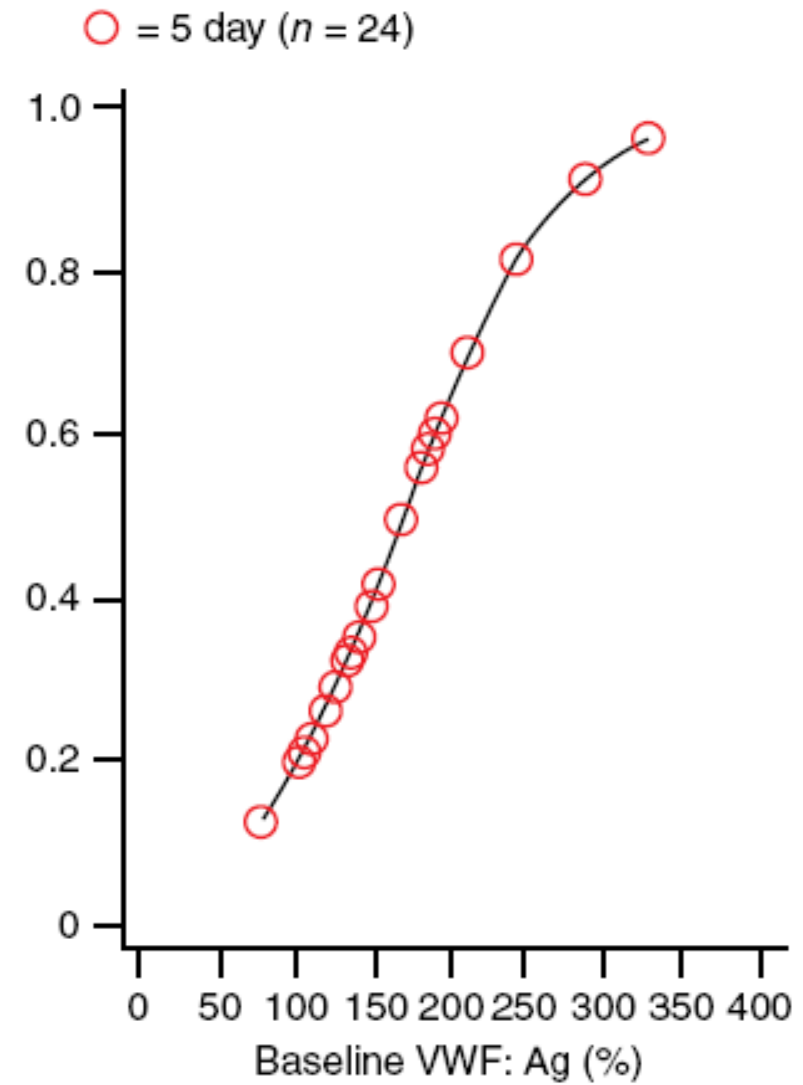
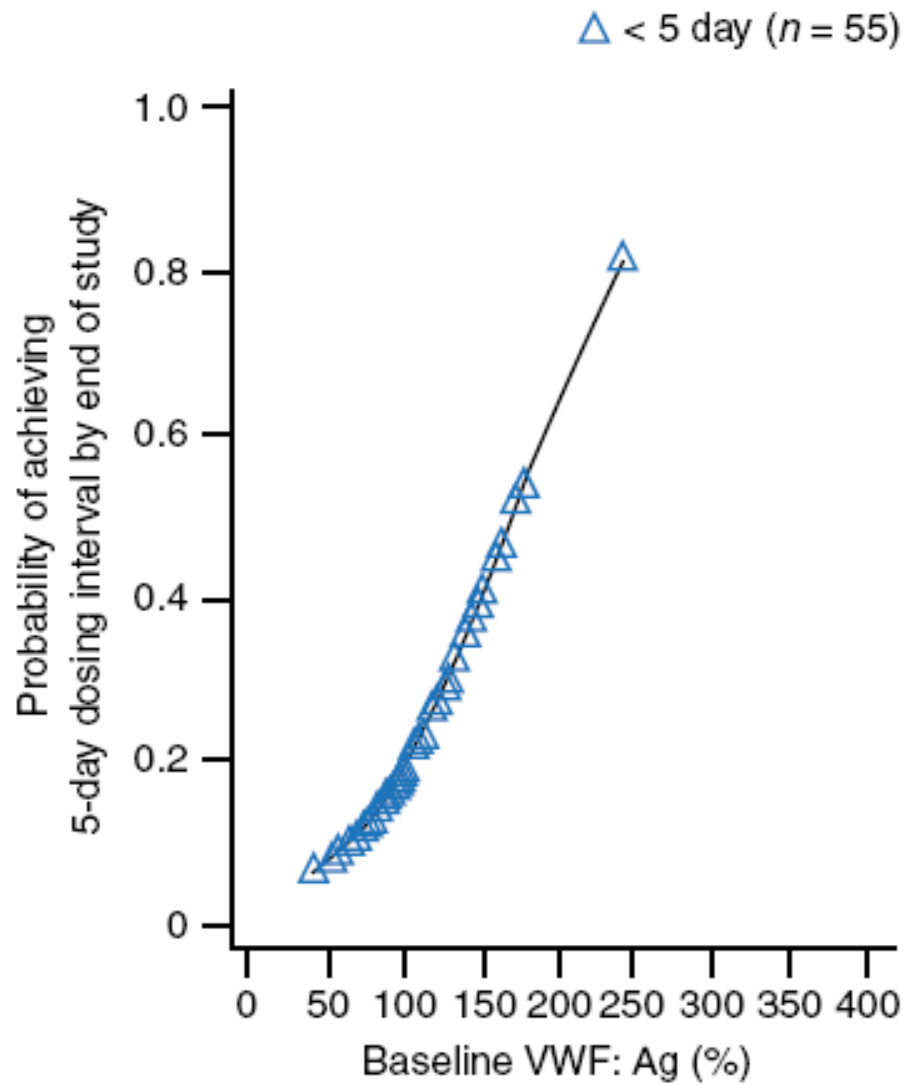
- **123 patients (≥ 12 yrs)**
- $t^{1/2}$: ~ 82 hours; IVR: 0.92
- Target trough: 1-3% or higher
- In the tailored prophylaxis arm 54% of patients were treated every 14 days
- No inhibitors were detected (55 pts with ≥ 50 EDs)
- No cases of anaphylactic reactions or thromboembolic events were reported

A-LONG: Phase 3 Study of rFVIIIFc in PTPs

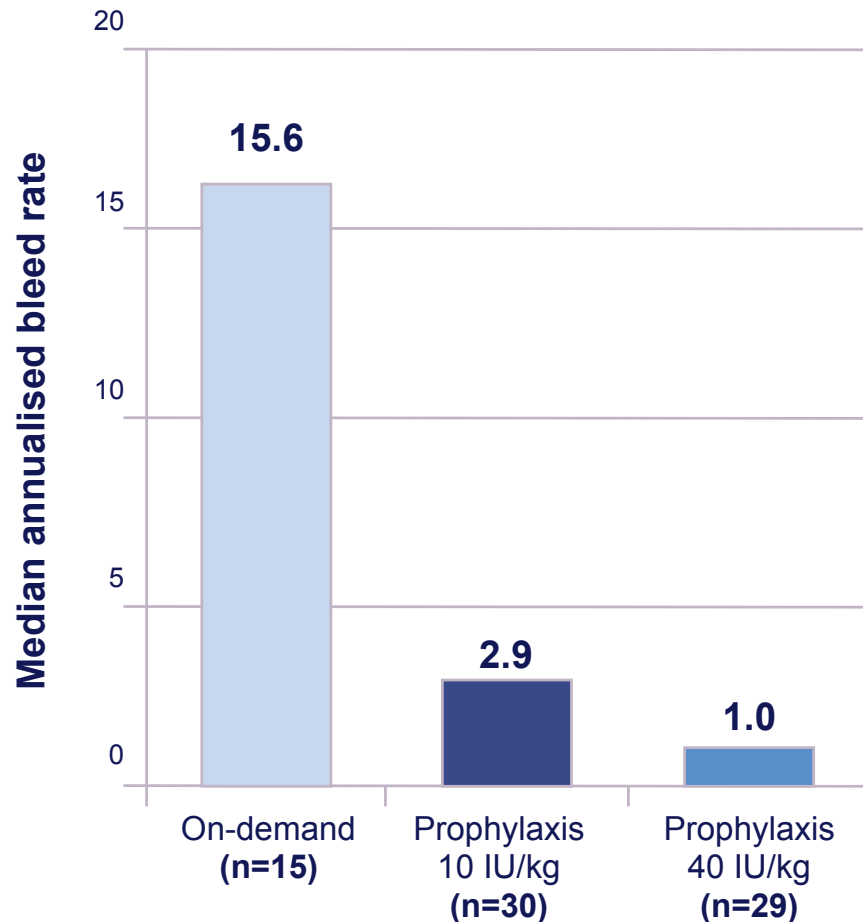
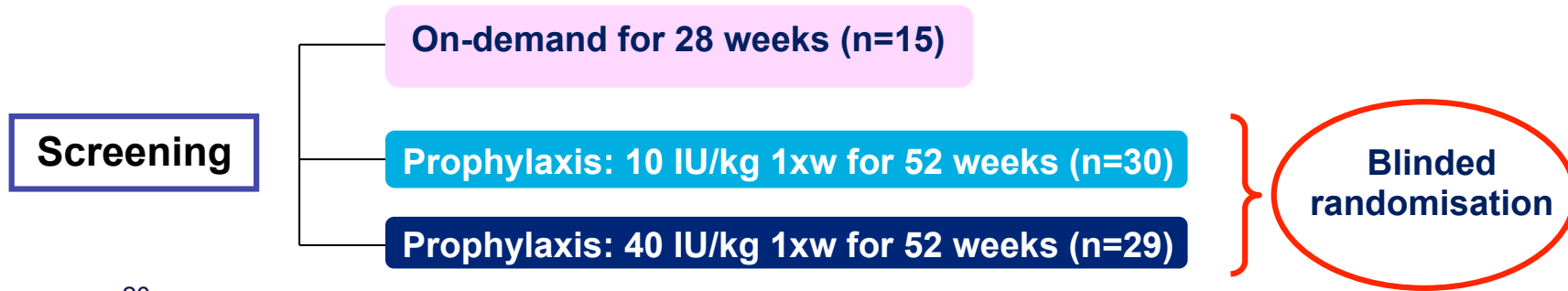


- **165 patients (≥ 12 yrs)**
- **$t^{1/2}$: 19.0 hours; IVR: 2.2**
- **Target trough: 1-3% or higher**
- **In the tailored prophylaxis arm the median weekly dose was 78 IU/kg**
- **30% of subjects achieved a 5-day dosing interval**
- **No inhibitors were detected (110 pts with ≥ 50 EDs)**
- **9 major procedures in 9 pts**

Post-hoc analysis on bleeding rates



Paradigm 2: Phase 3 study of N9-GP



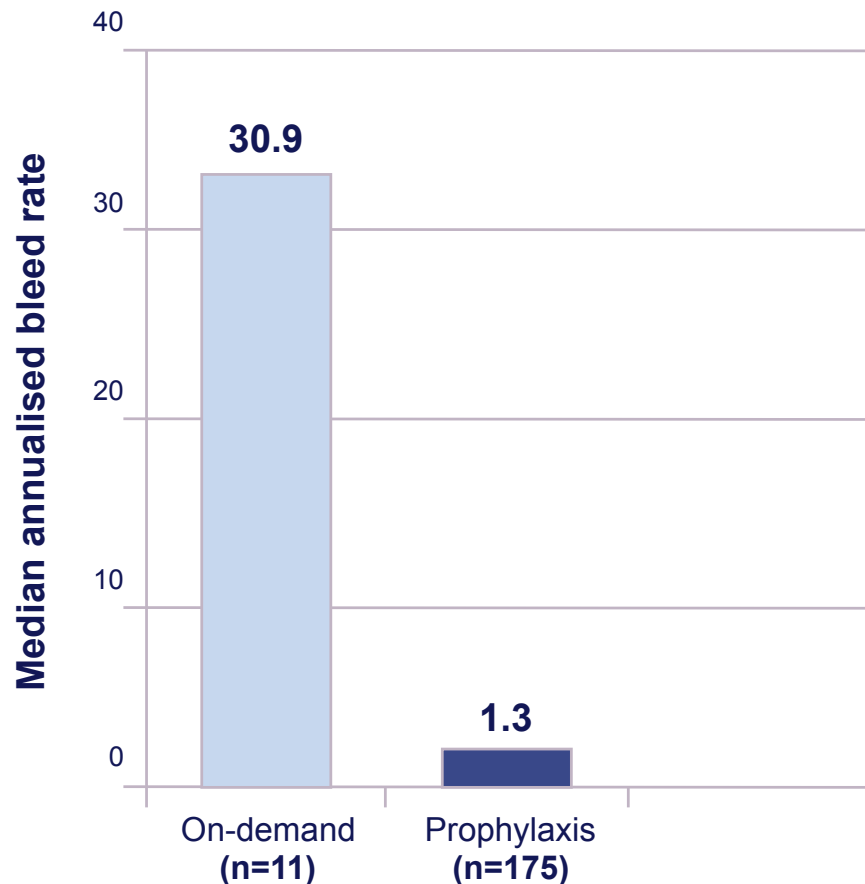
- $t^{1/2}$: 93 hours
- Overall success rate for treatment of bleeds: 92.4% (excellent or good)
- Bleeds were treated with a single dose of 40 IU/kg
- 91.7% of bleeds successfully treated with a single dose
- No inhibitory antibodies to N9-GP
- No safety issues

Pathfinder 2: Phase 3 Study of N8-GP

SCREENING

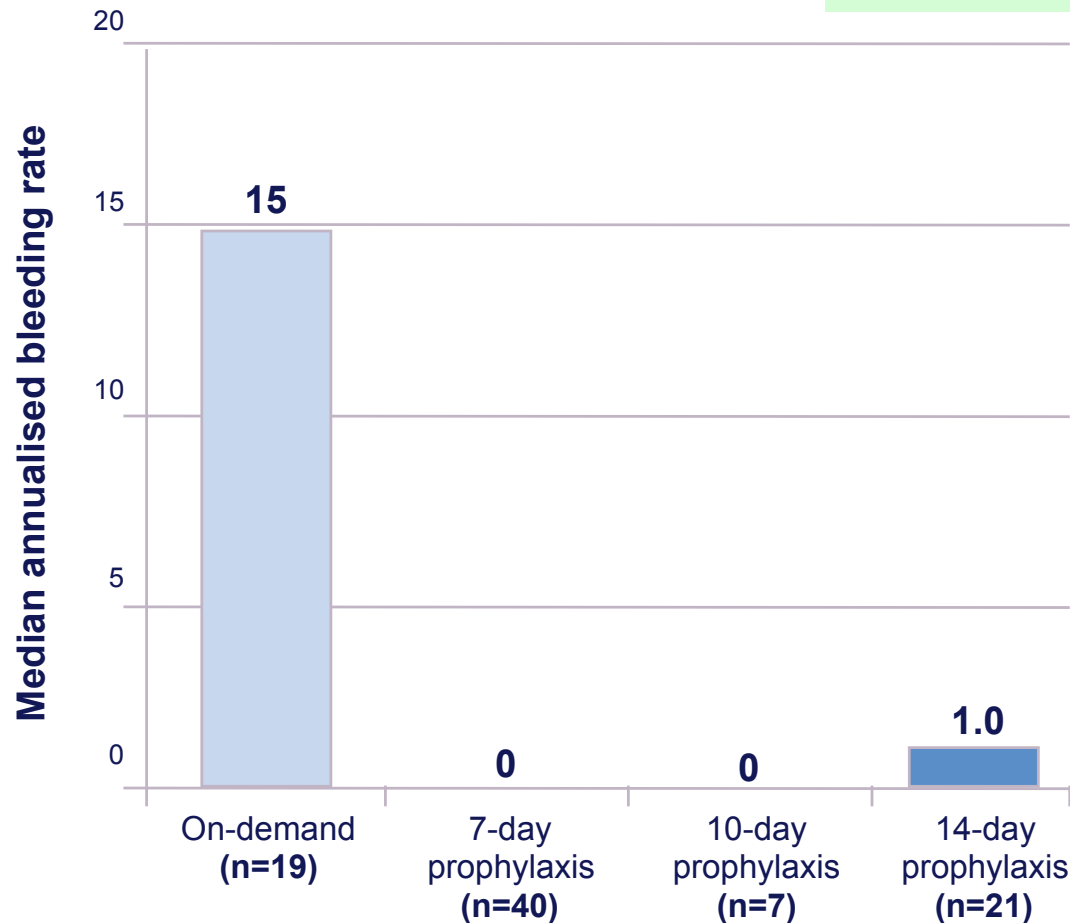
On demand (n=11)

Prophylaxis (50 IU/kg every 4 days) (n=175)



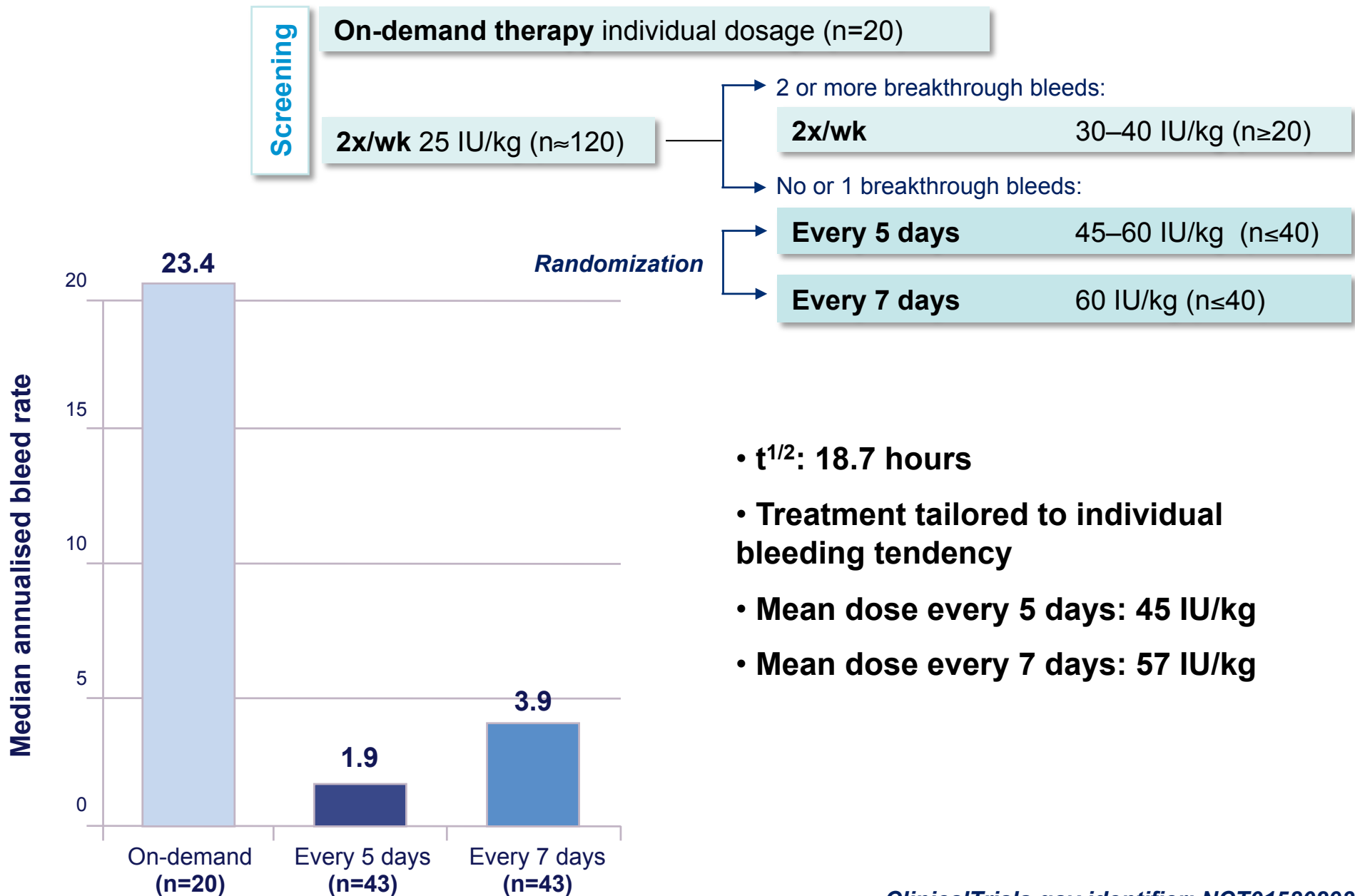
- $t^{1/2}$: 18.4 hours
- One patient developed anti-FVIII inhibitors
- Inhibitor development in line with expectations in PTPs (1 inhibitor)
- Mean trough level: 8%

Prolong9-FP: Phase 3 study of rIX-FP



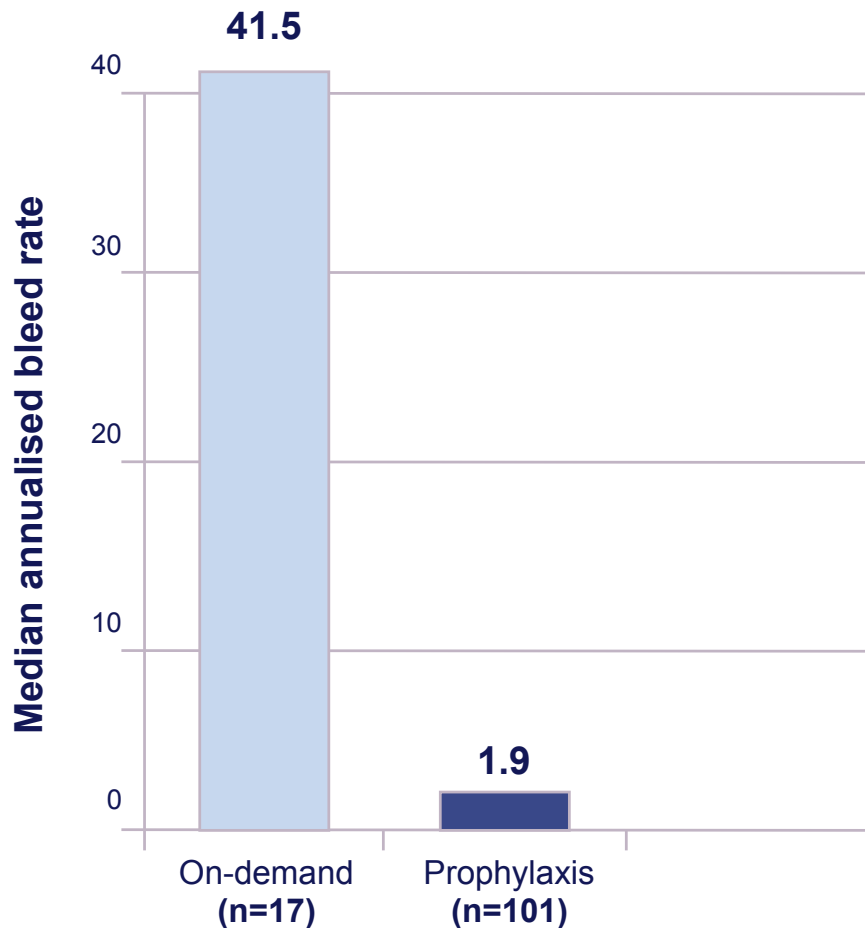
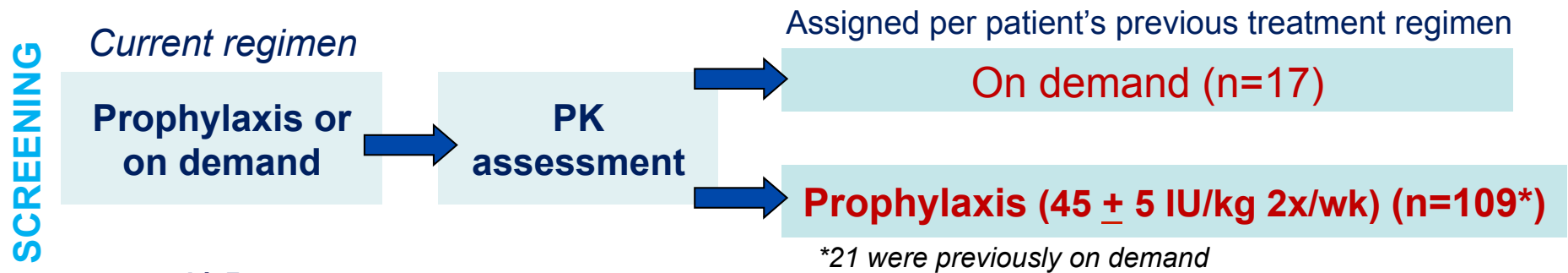
- *63 patients (≥ 12 yrs)*
- $t^{1/2}$: **102 hours**; IVR: 1.27
- No inhibitors were detected
- No cases of anaphylactic reactions or thromboembolic events were reported
- Mean trough: **20 IU/dL** (40 IU/kg/w)
- Mean trough: **12 IU/dL** (75 IU/kg/eow)

PROTECT-VIII: Phase 2/3 Study of BAY 94-9027 in PTPs



- $t^{1/2}$: 18.7 hours
- Treatment tailored to individual bleeding tendency
- Mean dose every 5 days: 45 IU/kg
- Mean dose every 7 days: 57 IU/kg

PROLONG-ATE: Phase 2/3 Study of BAX 855



- Full-length rFVIII covalently bound to a branched 20 kDa PEG moiety (random PEGylation)
- 60% of PEG localized on the B-domain
- Target trough: $\geq 1\%$
- $t^{1/2}$: 15 hours
- No inhibitor development

rFVIII a singola catena (CSL Behring)

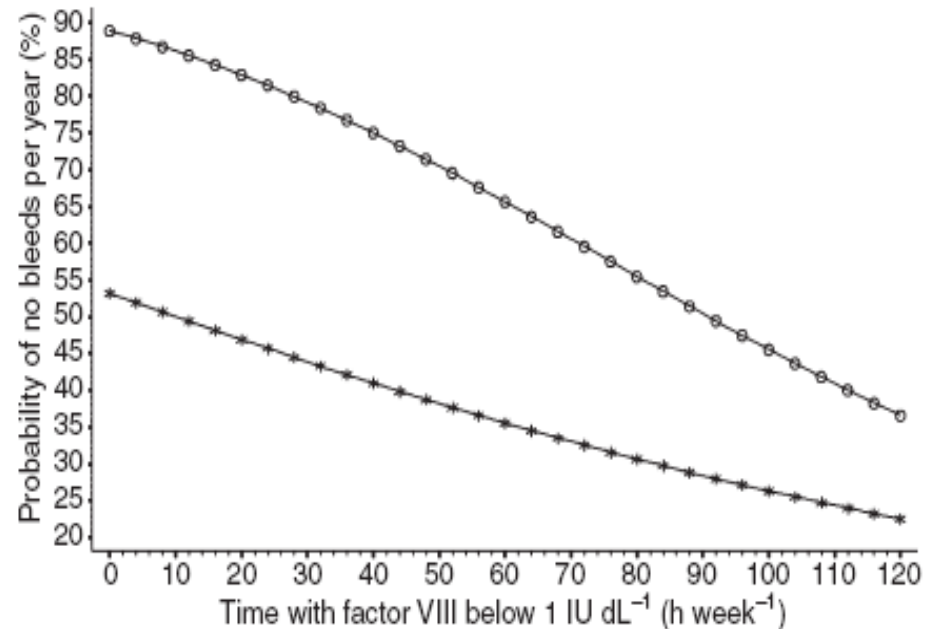
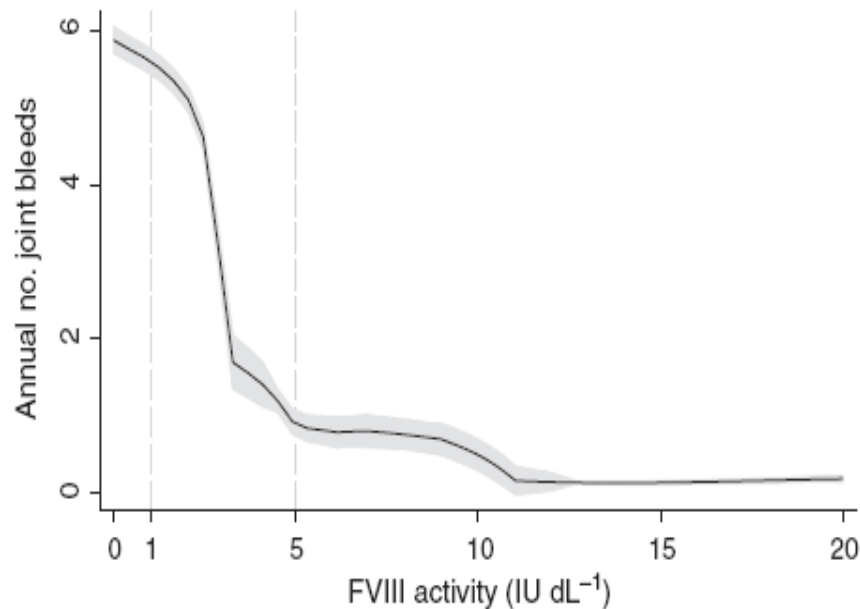
Aumentata stabilità della molecola dovuta a:

- Legame covalente tra catena leggera e catena pesante
- Espresso come FVIII a singola catena
- Maggiore integrità e stabilità molecolare dopo la ricostituzione
- La forma della singola catena si traduce in una maggiore affinità di legame con il vWF rispetto ad altri tipi di molecole di FVIII (potenziale effetto sull'immunogenicità)



Il ruolo del livello basale

- Nel passato livelli mantenuti tra 1 e 3% erano considerati “sufficienti”¹
- Per proteggere le articolazioni dagli ematridi sono necessari livelli più alti²
- Il rischio di emorragie intercorrenti è proporzionale al tempo in cui i livelli basali sono inferiori all'1%³





¹ Ahlberg A. *Acta Orthop Scand* 1965; 77 (Suppl): 3-132

² Den Uijl IE et al. *Haemophilia* 2011; 17: 849-53

³ Collins P et al. *JTH* 2009; 7: 413-20

Concentrati ad emivita modificata

Cambiamenti attesi riguardo ai regimi di profilassi

	Prodotti standard (n di infusioni/anno)		Prodotti ad emivita modificata (n di infusioni/anno)
Emofilia A	150-180		80-100
Emofilia B	100-120		30-40

A new era for haemophilia prophylaxis?

- Prophylaxis is the cornerstone of hemophilia therapy
- Primary prophylaxis in children without inhibitors is able to prevent overt joint damage
- Secondary prophylaxis is useful to improve quality of life and functioning in adult patients
- New long-acting products may facilitate prophylaxis feasibility and improve adherence to treatment regimens due to fewer injections
- New long-acting products may provide a better protection due to higher factor levels attained and maintained longer