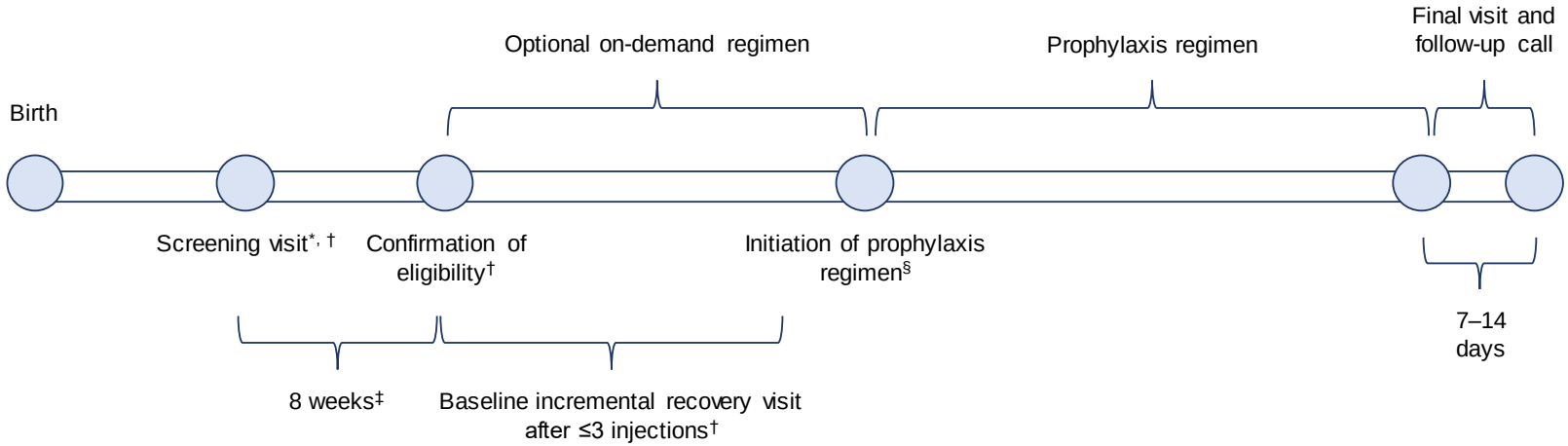
Supplemental Figure 1. Study design



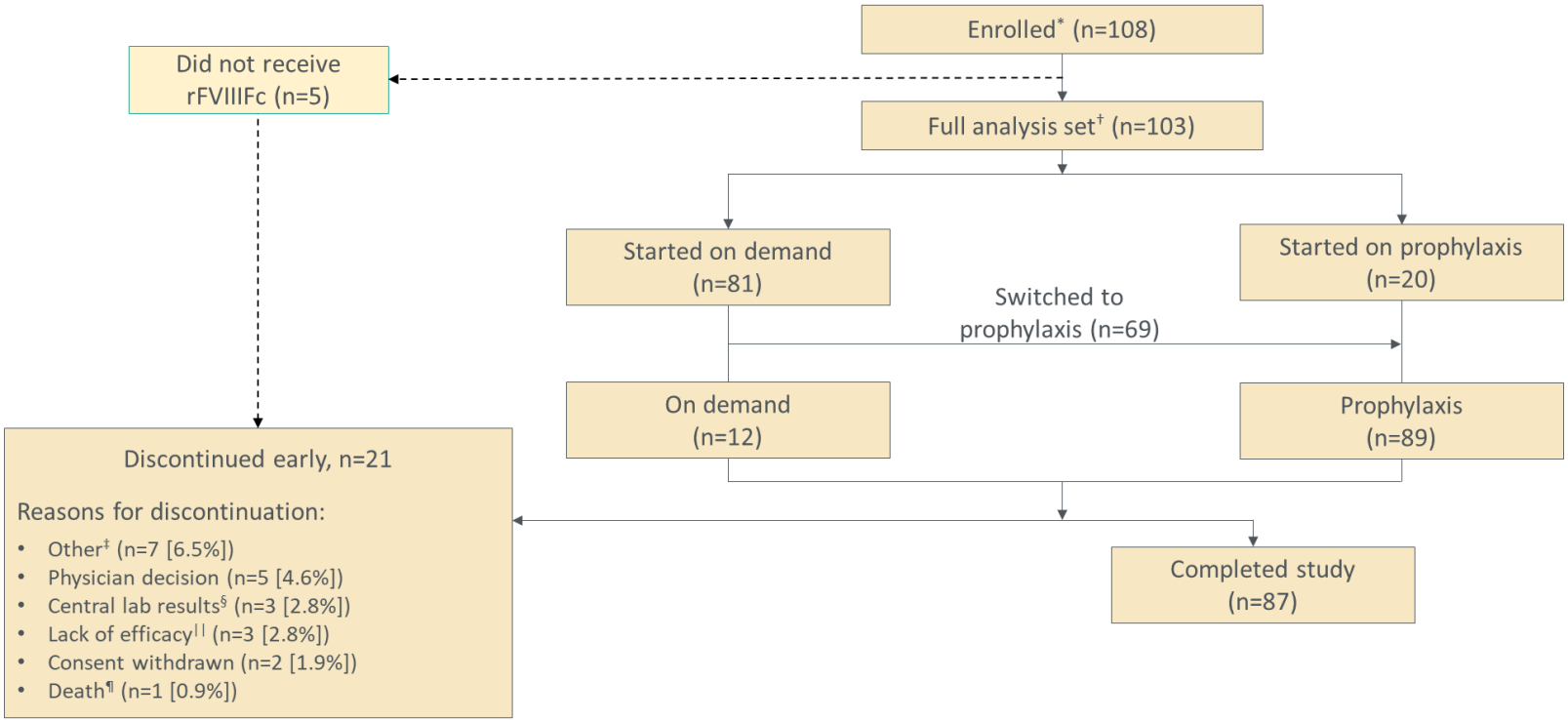
*Subjects were not allowed on study if they had received any infusion of factor prior to eligibility confirmation.

†Screening and baseline incremental recovery visits may be performed as 2 separate visits or all activities necessary for screening, confirmation of eligibility, and the baseline incremental recovery visit may be performed at the same visit.

‡When screening was not completed within 8 weeks, some assessments were repeated.

§Investigators had the option to treat a subject on demand, however, according to global standards of care, prophylaxis was generally initiated prior to or immediately following a third joint bleed.

Supplemental Figure 2. Subject disposition



rFVIIIFc, recombinant factor VIII Fc fusion protein; ITI, immune tolerance induction.

*All subjects who were enrolled in the study, whether or not dosed with rFVIIIFc.

†Enrolled subjects who had taken ≥1 dose of rFVIIIFc. Two subjects who discontinued early were not allocated to a treatment regimen.

‡Reasons included unavailable homecare (n=1), patient identified as meeting an exclusion criterion (n=2), discontinuation for need of continuous infusion (n=3 [n=2 for intracranial hemorrhage; n=1 for planned surgery]), and parent decision (n=1).

§Baseline FVIII activity level was determined to be ≥1% (screening failures).

||All 3 subjects had high-titer inhibitors and were receiving ITI at the time of discontinuation.

¶Death due to an intracranial hemorrhage during the screening period with onset before the first dose of rFVIIIFc.

Supplemental Table 1: Summary of risk factors by inhibitor classification[*,†]

Factor	High-titer inhibitor (n=14) n (%)	Low-titer inhibitor (n=14) n (%)
Race		
Black or White Hispanic (n=5)	2 (40.0)	3 (60.0)
Other (n=23)	12 (52.2)	11 (47.8)
Family history of inhibitor		
Yes (n=9)	6 (66.7)	3 (33.3)
No (n=15)	6 (40.0)	9 (60.0)
Unknown (n=4)	2 (50.0)	2 (50.0)
Genotype		
High risk (n=23)	11 (47.8)	12 (52.2)
Low risk (n=1)	0 (0.0)	1 (100.0)
Unknown risk (n=4)	3 (75.0)	1 (25.0)
Treatment emergent adverse event of infection		
Yes (n=17)	9 (52.9)	8 (47.1)
No (n=11)	5 (45.5)	6 (54.5)

rFVIIIFc, recombinant factor VIII Fc fusion protein.

[*]Percentages are based on the number of subjects at each level of the risk factor.

[†]Subjects developing a positive inhibitor (≥0.6 BU/mL, confirmed by a second test result from a separate sample drawn ≥2 weeks after the date of the original sample) after exposure to rFVIIIFc are included in the inhibitor subgroup.