P-M-150

Longitudinal Analysis of Annualized Bleeding Rates Among Adults/Adolescents Receiving Weekly Prophylaxis With rFVIIIFc in A-LONG and ASPIRE

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INTRODUCTION

- Recombinant factor VIII Fc fusion protein (rFVIIIFc) was developed to have a prolonged half-life compared with conventional factor VIII (FVIII) products[1-4]
- The safety, efficacy, and prolonged half-life of rFVIIIFc were demonstrated in the Phase 3 A-LONG study[5] (ClinicalTrials.gov Identifier: NCT01181128) and in the ongoing ASPIRE extension study (NCT01454739; interim ASPIRE results have been published[6])

OBJECTIVE

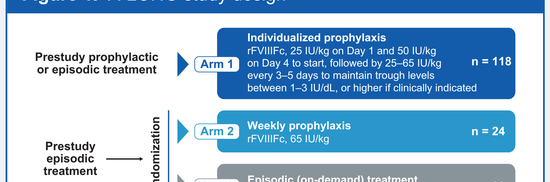
- To report longitudinal annualized bleeding rates (ABRs) in subjects receiving once-weekly prophylaxis in A-LONG and/or the ongoing rFVIIIFc extension study ASPIRE, as of the first interim data cut (January 6, 2014)

METHODS

Study Design

- Previously treated males (≥12 years of age) with severe hemophilia A (<1 IU/dL endogenous FVIII activity) were eligible for A-LONG (Figure 1)

Figure 1. A-LONG study design



- Subjects who completed A-LONG could participate in 1 of 4 treatment groups in ASPIRE (Table 1)
  - Subjects could change treatment groups at any point in ASPIRE; thus, subjects could be represented in >1 treatment group
- These analyses included all data from the weekly prophylaxis groups of A-LONG and ASPIRE (as of the first interim data cut on January 6, 2014) for subjects who received ≥1 dose of rFVIIIFc; for subjects who enrolled in ASPIRE subsequent to completing A-LONG, cumulative data were used

Table 1. ASPIRE treatment groups

Treatment group	Dosing guidance per protocol
Individualized prophylaxis	rFVIIIFc 25–65 IU/kg every 3–5 days, OR twice-weekly rFVIIIFc (20–65 IU/kg on Day 1, 40–65 IU/kg on Day 4)
Weekly prophylaxis	rFVIIIFc 65 IU/kg every 7 days
Modified prophylaxis[a]	Investigators could personalize dosing for subjects in whom optimal prophylaxis[a] could not be achieved with individualized or weekly prophylaxis (eg, less frequent dosing, targeting a FVIII trough level of >3 IU/dL)
Episodic treatment	rFVIIIFc dosing based on type and severity of bleeding episode

PK = pharmacokinetics.
[a]Dosing was optimized according to the subject's clinical profile and/or individual PK; the need for additional dose adjustment was based on physician/patient judgment.

RESULTS

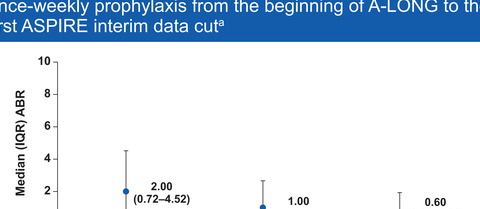
Study Population

- From the beginning of A-LONG to the first ASPIRE interim data cut, the median cumulative treatment time with rFVIIIFc among subjects who were ever on weekly prophylaxis (n = 37) was 1.51 (range, 0.02–2.08) years
  - The classification "ever on weekly prophylaxis" defines any subject who was ever recorded as having been included in the weekly prophylaxis treatment group with evaluable efficacy data
- The median cumulative treatment time with rFVIIIFc among subjects who remained on weekly prophylaxis from the beginning of A-LONG through the first ASPIRE interim data cut (n = 17) was 1.99 (range, 0.02–2.08) years
- As of the first interim data cut of ASPIRE, of the 19 subjects who were on weekly prophylaxis at the end of A-LONG, regardless of treatment group designation, 16 subjects were dosing once weekly (including 13 in the weekly prophylaxis group and 3 in the modified prophylaxis group)

Annualized Bleeding Rates

- Median on-study ABRs were low among subjects who were ever on once-weekly prophylaxis (Figure 2)

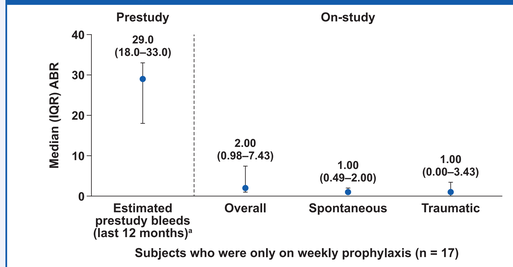
Figure 2. Cumulative ABRs among subjects who were ever on once-weekly prophylaxis from the beginning of A-LONG to the first ASPIRE interim data cut[a]



IQR = interquartile range.
[a]For subjects who were ever on once-weekly prophylaxis, ABR data were evaluated for the time during which the subject was on weekly prophylaxis.

- Among the 17 subjects who were only on weekly prophylaxis during A-LONG and/or ASPIRE, median ABRs were low (Figure 3)

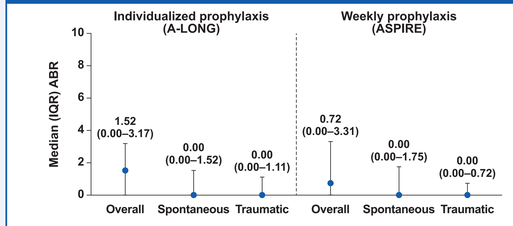
Figure 3. Prestudy and cumulative on-study ABRs among subjects who were treated episodically pre–A-LONG and remained on once-weekly prophylaxis from the beginning of A-LONG through the first ASPIRE interim data cut



[a]Only overall ABRs were assessed in the 12 months prior to A-LONG.

- Among the 9 subjects who switched from individualized prophylaxis to weekly prophylaxis during A-LONG/ASPIRE, bleeding rates generally remained low with once-weekly prophylaxis (Figure 4, Table 2)

Figure 4. Cumulative ABRs among subjects who were in the individualized prophylaxis group during A-LONG and switched to the once-weekly prophylaxis group during ASPIRE[a]



[a]The median dosing interval was 3.50 days during the last 3 months in A-LONG for subjects on individualized prophylaxis.[5]

Table 2. Subject-level comparison of ABRs for subjects who switched from individualized prophylaxis to weekly prophylaxis during A-LONG/ASPIRE[a]

	Individualized prophylaxis		Weekly prophylaxis	
Subject #	Efficacy period (y)	ABR	Efficacy period (y)	ABR
1	0.76	0.0	1.38	0.7
2	0.48	4.2	1.51	3.3
3	0.42	2.4	1.47	0.0
4	0.90	3.3	1.14	4.4
5	0.58	0.0	1.50	0.0
6	0.82	1.2	1.31	0.8
7	0.60	0.0	1.51	0.0
8	0.63	3.2	1.67	0.6
9	0.66	1.5	1.45	4.1

[a]Subjects who maintained the same or had a decreased ABR upon switching to weekly prophylaxis are shown in white.

LIMITATIONS

- Analyses of ABRs among subgroups that received once-weekly prophylaxis during A-LONG and/or ASPIRE were based upon relatively small sample sizes
- Among subjects who switched from individualized to weekly prophylaxis, the total duration of time on weekly prophylaxis may be shorter than on individualized prophylaxis, as of the first ASPIRE interim data cut

CONCLUSIONS

- The results of this analysis demonstrate that subjects dosing once weekly with rFVIIIFc during A-LONG/ASPIRE maintained low ABRs over an extended time period
  - Median overall ABRs were ≤2.00 and median spontaneous and traumatic ABRs were ≤1.00 in various subgroups of subjects on weekly prophylaxis during A-LONG/ASPIRE
  - For some subjects, once-weekly prophylaxis was just as effective in preventing bleeding episodes as individualized prophylaxis (median dosing interval with individualized prophylaxis during A-LONG, 3.50 days[5])
- Results from this subset of subjects from A-LONG/ASPIRE suggest that once-weekly prophylaxis can prevent bleeding episodes and may be an appropriate option for a subset of patients

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Disclosures

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