Comparison of paper diary and B-CoNect (telemetric smartphone application) at home treatment monitoring of severe hemophilia A patients

Marianne Sigaud[1], Valérie Horvais[2], Valérie Chamouard[3], Benoît Guillet[4], Thierry Lambert[5], Annie Borel-Derlon[6], Claude Négrier[7], Edita Dolimier[8], Anne-Marie Masquelier[9].

[1] Haemophilia Treatment Center, Nantes University Hospital, Hôtel-Dieu, Nantes, France - [2] Pharmacy Department, Nantes University Hospital, Hôtel-Dieu, Nantes, France - [3] Pharmacy Department, Louis Pradel Hospital, Lyon, France - [4] Haemophilia Treatment Center, Rennes University Hospital, Pontchaillou, Rennes, France - [5] Haemophilia Treatment Center, Le Kremlin-Bicêtre Hospital, Paris, France - [6] Haemophilia Treatment Center, Caen University Hospital, Caen, France - [7] Haemophilia Treatment Center, Louis Pradel Hospital, Lyon, France - [8,9] Baxter Healthcare Corporation, Maurepas, France.

Introduction and objectives

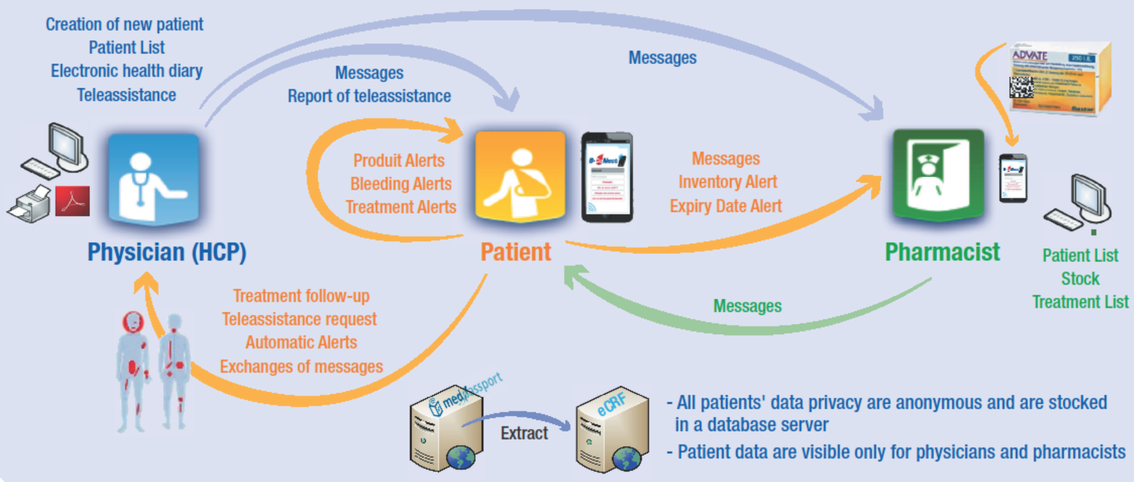
Hemophilia is a rare hereditary bleeding disorder caused by a deficiency in coagulation factor(s). Nowadays, therapeutic strategy is based on substitutive therapy with coagulation factors by patients, their family members or nurses on a home treatment basis.

Patients fill out paper diaries, describing the frequency of bleeding episodes, the circumstances of medication administration, the adverse events. These diaries, however, provide only retrospective follow-up and information on past treatment, but no visibility on patient's status day by day in real time. Several clinical studies [1,2] showed that data recording methods via electronic device are equivalent or superior to paper support. Remote medical monitoring devices permit medical team to interpret patients' data in real time, and to adjust therapy strategy if needed.

B-CoNect is a telemetric smartphone application which allows patients with **Co**agulation problems to be con**Nected** via an electronic diary with the hemophilia health care team (physicians and pharmacists) *(fig. 1)*.

This prospective, interventional, randomized in, crossover pilot **B-CoNect** study, evaluated the interest of **B-CoNect** e-diary versus paper diary for data recording and treatment compliance. We present here the results of the interim analysis.

Figure 1. B-CoNect organization



Methods

Study design

- B-CoNect is a prospective, interventional, multicenter, and randomized in crossover pilot study, conducted in 4 hemophilia treatment centers (HTC) in France, with a total enrolment of 29 patients.
- Each patient included was randomized in one of the two predefined groups *(fig. 2)*:
  - Group 1: treatment monitoring with electronic diary then followed by the classic paper diary;
  - Group 2: treatment monitoring with classic paper diary then followed by the electronic diary.
- Patients were selected (selection visit) and then followed for 6 months maximum through 3 visits: initiation visit, 3 months follow up visit where patients switched between electronic and paper diary and closeout visit at 6 months. Telephonic contacts were also performed by the clinical research associate of investigational sites.

Inclusion criteria

Patients were eligible to the study if they had all of the following criteria:

- Male or female patient 2 years of age or older;
- Patient with severe Hemophilia A (FVIII≤ 2%), without inhibitor, treated by ADVATE®;
- Patient with regular treatment, at least once per month during the last three months before enrolment in the study, independently of therapeutic plan;
- Patient with hemophilia diary filled at least partially during the last month before inclusion;
- Patient receiving ADVATE® in retrocession;
- Patient, his/her parents or legal representatives being present at the training of e-diary use and understanding it;
- Patient, his/her parents or legal representatives being informed on the content of the study and signing the written consent form.

Non-inclusion criteria

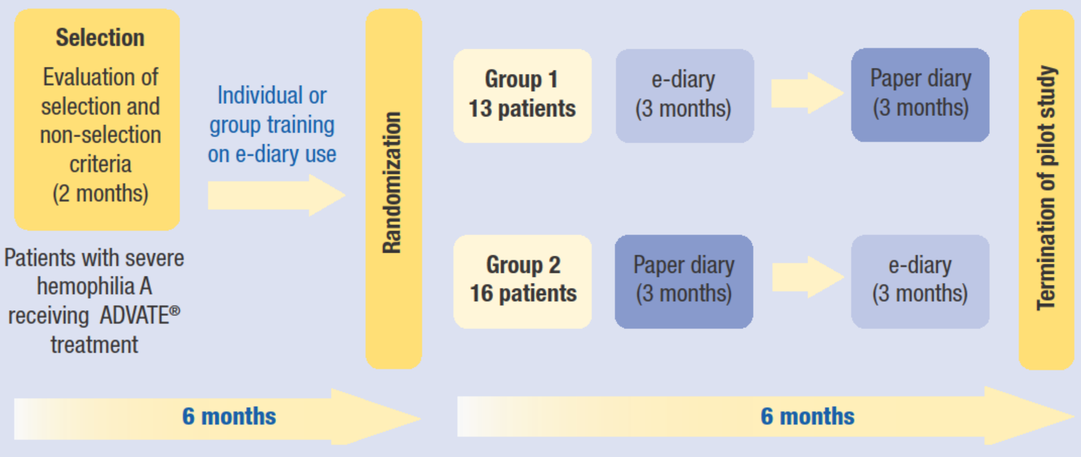
Patients were not included in the study if they had one of the following criteria:

- Patient participating in another interventional study;
- Patient with immune tolerance induction (ITI) in progress;
- Patient, his/her parents or legal representatives being unable to attend training of e-diary use or unable to understand it.

Evaluation criteria

- Primary endpoint: the primary endpoint was the rate of diary completion regarding the reason of each injection.
- Secondary endpoints: the secondary endpoints were the following:
  - Completion rate of details about bleeding (date; hour; localization; spontaneous or traumatic bleeding);
  - Rate of traceability of administered medication;
  - Rate of global diary completion;
  - Rate of completion of information on substitutive treatment (date; hour; etc.);
  - Number of warnings sent to the physician;
  - Number of warnings sent to the pharmacist;
  - Number of patient-physician messages generated;
  - Number of physician-patient messages generated;
  - Number of patient-pharmacist messages generated;
  - Number of pharmacist-patient messages generated;
  - Total number of not scheduled consultations due to the real time monitoring;
  - Total number of consultations generated following message/warning/photo/video sending;
  - Patient's, physician's and pharmacist's satisfaction survey;
  - Number of demands of IT (Information technology) assistance.

Figure 2. Study flow-chart



Results and conclusions

Patients' characteristics at enrolment

29 male patients of 27.7 +/- 16.7 years mean age were enrolled in the study. 60% of these patients were less than 30 years old.

13 patients formed group 1 (e-diary for the first 3 months, paper diary afterwards) and 16 patients formed group 2 (paper diary for the first 3 months, e-diary afterwards).

In 82.8% of cases, patients themselves used the electronic device; moreover, 89.3% of patients had experience of electronic device use and 64.3% had experience of smartphone use. More than 65% of patients enrolled were treated with ADVATE® for prophylaxis with median dose of 2000 IU/injection at a mean frequency of 2.5 injections/week.

Interestingly, physicians have evaluated the paper diary completion by patients during the last month before their enrolment in the study; results showed that the exact hour of treatment, the date and hour of bleeding were often described less than once in two.

Primary endpoint

The primary endpoint was the rate of electronic and paper diary completion regarding the reason of injections. The aim of primary endpoint analysis was to demonstrate the non-inferiority of e-diary versus the paper diary regarding this subject.

The difference in the adjusted mean of the intra-individual difference of the reason of injection completion rate between paper and e-diary was: -19.5 (95% CI -38.1 to -1.0). Since the upper bound of the 95% confidence interval is inferior to the non-inferiority threshold (0.1), we concluded to the non-inferiority of e-diary vs paper diary.

Otherwise, an ANOVA performed on the adjusted mean of the intra-individual difference showed a significant impact of the diary support (electronic or paper) on the completion rate of the reason of injections (p=0.0398) with an average completion rate of 96.3% with e-diary and 76.8% with paper diary *(fig. 3)*. We noted that the paper diary completion rate was better when used after the e-diary completion but this difference was not statistically significant (p=0.1960) *(fig.4)*. The specific effect related to the patient had no significant impact on the diary completion rate (p=0.5552).

Secondary endpoint

Participants' satisfaction with e-diary (physicians, pharmacists and patients) was one the secondary endpoints of this pilot study.

Patients' satisfaction *(Figure 5)*

79.2% of patients were satisfied or very satisfied with the application **B-CoNect.**

75% of patients found this electronic support very easy in use. Particular advantages of this device were the possibility to easily manage and update treatment stock (appreciated by 87% of patients), to send (to) and receive real time messages from their physicians (64.3% of patients satisfied or very satisfied), to receive immediate care in case of emergency (70% of patients were satisfied or very satisfied).

As mentioned earlier, patients were enrolled in the study independently of their therapeutic ADVATE® regimen. An important observation was that 57.1% of patients on prophylaxis regimen certified that the use of electronic tool improved the frequency and regularity of the injections.

Some patients mentioned that the price of an IPhone may become a preventing factor for wide e-diary use. But, despite of it, 71% of patients were willing to replace the paper diary by the e-diary and 75% of them were willing to encourage other patients to use it.

Physicians' satisfaction

Unfortunately, at this interim analysis, only 3 investigation centers out of 4 answered to the satisfaction survey. 66.7% of physicians were satisfied with the monitoring of patients through the application, noting the necessity of slight changes, in order to receive more detailed and precise information from the patients for a better follow-up.

Pharmacists' satisfaction

Regarding the pharmacists, 75% were satisfied with ADVATE® stock traceability; although these conclusions are preliminary, taking into account the low number of professionals who responded to the satisfaction survey.

Figure 3. Average completion rate of e-diary and paper diary regarding the injection reason (%)

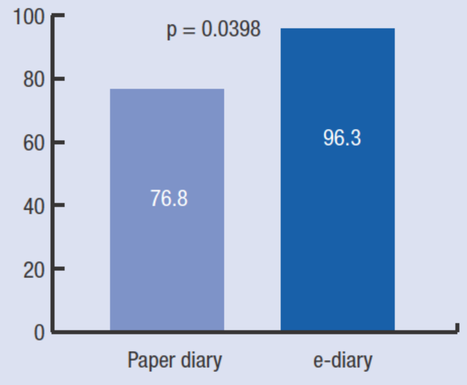


Figure 4. Diary completion rate regarding the sequence of use of the two diary supports

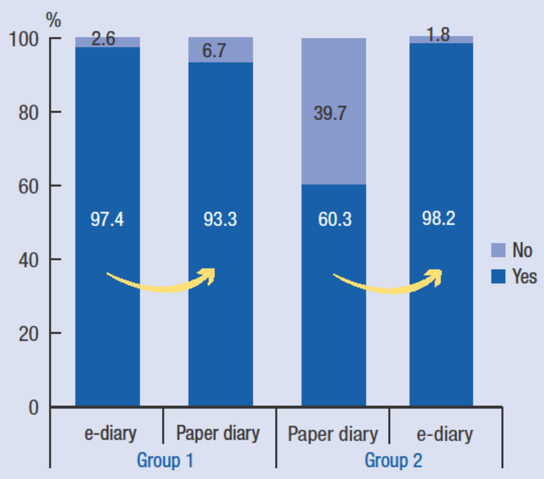
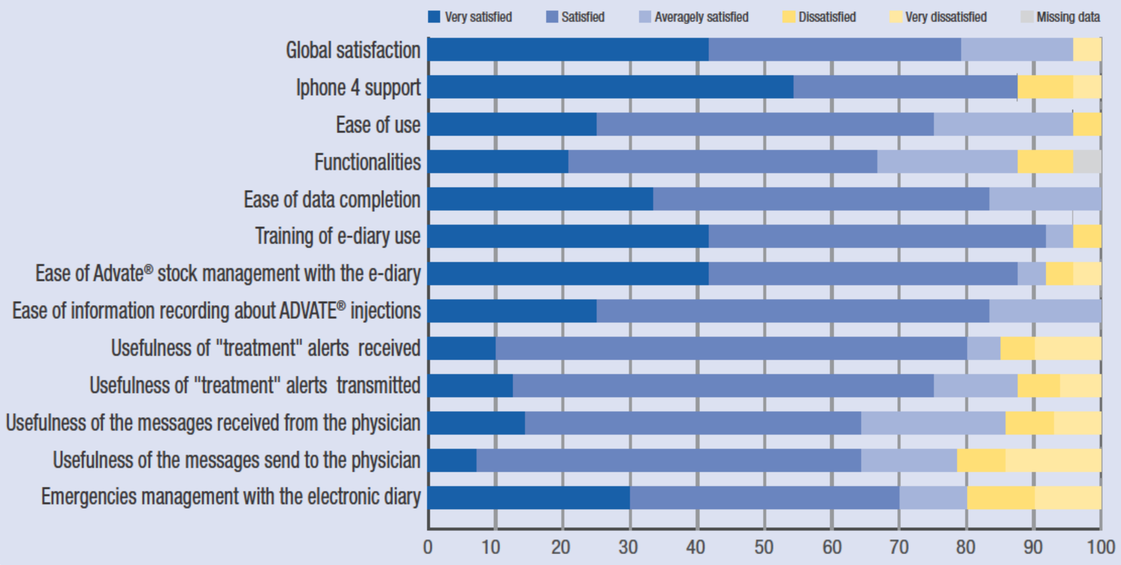


Figure 5. Patients' satisfaction with the electronic diary



Reference

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Conclusions

- **This pilot study clearly demonstrates the value of B-CoNect for home treatment monitoring of severe hemophilia A patients treated with Advate®.**
- **It also aimed to identify the application's points to improve. Based on the results of patients', physicians' and pharmacists' satisfaction surveys, necessary improvements will be performed. All these changes will be taken into account for the next steps.**

Presented at the WFH 2014 World Congress in Melbourne, Australia • May 11-15, 2014

If you have any additional questions, please feel free to contact Baxter Bioscience Medical Information at medinfo@baxter.com

Conflicts of interest: B-CoNect Study funded by BAXTER • Acknowledgments: This study and this poster were supported by the B-CoNect study group and by funding from BAXTER.

DOI: 10.3252/pso.eu.WFH2014.2014