A savvy approach to clinical trial recruitment for the SAAVY (Seroprevalence of AAV AntibodY) study in the era of COVID-19: Designing for a prospective, observational study in the United States during a global pandemic

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Background

- Adeno-associated virus (AAV)-mediated gene therapy is being investigated as a treatment for people with hemophilia A (PwHA).
- AAV serotypes commonly studied as potential vectors for gene therapy include AAV5, AAV6, and AAV8.
- Pre-existing immunity against AAVs restricts patient eligibility[1–3], yet published data on AAV seroprevalence and seroconversion rate in PwHA are limited.

AIMS

We describe the design and recruitment methods used for the SAAVY study (BMN 270-701), which aims:

- To characterize AAV antibody prevalence and titers, evaluate changes in antibody titer over 3–6 months, and examine factors that may influence antibody positivity, titer, and seroconversion.
- To minimize the need for in-person study interactions during the COVID-19 pandemic.

Table 1. Virtual outreach methods

Recruitment Efforts

- SAAVY website
- SAAVY mobile application
- Partner email outreach
- Online recruitment [advertising] initiatives

Community Awareness Campaign

- HCP Educational Webinars
- SAAVY Advisor Videos
- Infographic Brochures
- Patient Advocacy Group (PAG) engagement

Methods

- SAAVY is a **patient-centered, decentralized randomized, prospective, observational study** involving blood draws at two time points.
- SAAVY employs **unified virtual study coordination** and a user-friendly mobile app to enable remote recruitment across the US.
- Biospecimen samples are collected through a network of 1,800+ laboratories throughout the US.
- This approach removes burden of performing study assessments from hemophilia treatment center (HTC) staff, minimizes patient travel, and has allowed for mitigation of potential exposure to COVID-19.
- Recruitment has leveraged various forms of virtual outreach to create awareness of the study and its scientific aims (**Table 1**).
- Study procedures are outlined in **Figure 1**.
- A central Call Center team acts as virtual study coordinators, together with a central Primary Investigator (PI), to provide support to participants and to assist with the management of blood draws at local Patient Service Centers (PSCs) (**Figure 2**).

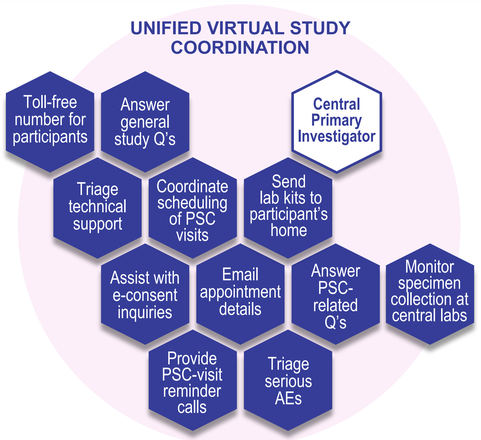
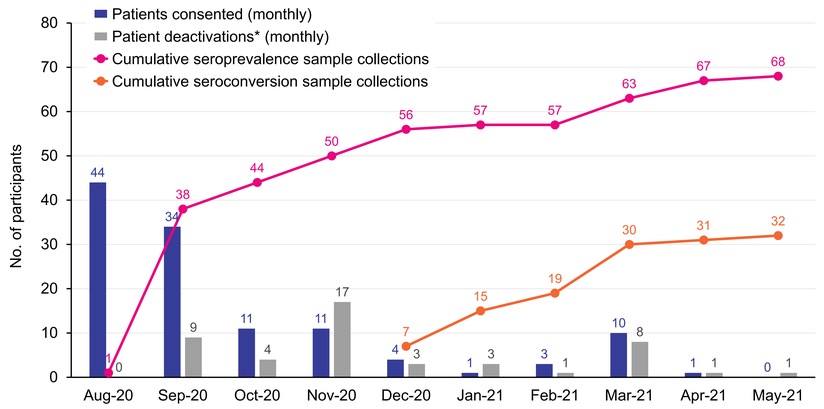


Figure 2. Unified Study Coordination Responsibilities
AE, adverse event; PSC, Patient Service Center; Q, question.

Current Enrollment Status



*The majority of deactivations were consented patients who were unable to be contacted to schedule a visit (LTF) or who did not attend their visits and later became unreachable.

Other reasons were:

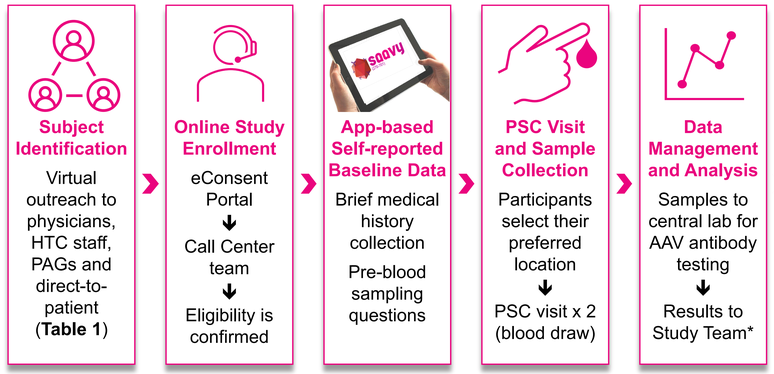
- No PSC nearby (4)
- Did not want to participate further (2)
- Patient died (unrelated to study procedures) (1)
- Moved away (1)
- Concerns relating to COVID-19 (1)

Figure 3. SAAVY [270-701] Enrollment and Sample Collections

LTF, lost to follow-up; PSC, Patient Service Center

- As of May 2021, 68 PwHA are actively involved in the study out of 119 total consented (**Figure 3**). The first enrollment occurred within 4 months of final protocol; 41 participants were enrolled within 2 weeks of start.
- The study was designed before the outbreak of the COVID-19 global pandemic, when a target sample size of 1,000 PwHA was considered feasible.
- Restrictions imposed by the pandemic have slowed recruitment, even with the use of virtual outreach programs and decentralized services. Advantages and challenges are summarized in **Table 2**.
- Experience in this study illustrates the importance of clearly defined patient recruitment and retention strategies to support decentralized trials.

Seroprevalence of AAV antibody (SAAVY), is a prospective, observational study evaluating rates of seroprevalence and seroconversion of antibodies to AAV serotypes in PwHA in the United States



*And to participants' physicians (if participants have consented to share their data)

Figure 1. Study Implementation

Table 2. Recruiting for a Clinical Trial in a Virtual Environment: Advantages and Challenges

Advantages	Challenges
Minimizes participants' travel, reduces potential exposure to COVID-19	Perceived value and relevance of the study may be reduced amid concerns and challenges of the pandemic
Only sample collection requires face-to-face contact with facility	Fewer visits to HTCs/PAGs reduces opportunity for dialog
The study is led by a single PI and utilizes a central IRB	Relies on motivated HTC staff to share information with patients and proactively follow up to minimize LTF
HTCs do not require local institutional IRB review/approval	Relies on motivated patients to navigate enrollment and engage with study procedures at multiple time points
HTCs do not need to be involved with sample collection/shipment/ processing or data entry	Relies on transfer of samples from commercial PSCs, not necessarily familiar with study procedures/GCP
	Relies on self-reporting of data by participants
	Time-limited environment for discussions with HTCs in a tele-health setting imposed by COVID-19 restrictions

AAV, adeno-associated virus; GCP, Good Clinical Practice; HTC, hemophilia treatment center; IRB, institutional review board; LTF, lost to follow-up; PAG, patient advocacy group; PI, Principal Investigator; PSC, Patient Service Center

CONCLUSIONS

- The COVID-19 pandemic has disrupted the progress of clinical studies worldwide.
- The design of SAAVY and initial outreach were implemented prior to shelter-in-place orders; revised outreach initiatives adapted for the situation have brought a ~12% success rate in the most challenging period of the pandemic.
- This success was achieved without traditional marketing campaigns or recruitment strategies and was based on systems enabling close communication between PwHA and HTCs/PAGs.
- Careful study design and multi-modal engagement with the hemophilia community can facilitate the conduct of studies, minimize risks associated with COVID-19, and may enhance patient experience and clinical trial recruitment.

Acknowledgments

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