RESEARCH ARTICLE

Advocate involvement in Clinical Trials: Lessons from the Patient-centric I-SPY2 Breast Cancer Trial

Jane Perlmutter[1], Susie Brain[1], Thelma Brown[1], Deborah Collyar[1], Amy Delson[1], Diane Heditsian[1], Barbara LeStage[1], Bev Parker[1], Susan Samson[1], Joan Venticinque[1], Jeff Matthews[2]

[1] I-SPY Patient Advocate
[2] Quantum Leap Heathcare Collaborative

Corresponding author: janep@gemini-grp.com

ABSTRACT
The innovative I-SPY2 Breast Trial is presented as an example of an unusually patient-centric clinical trial that has been significantly impacted by extensive advocate involvement. By describing how advocate involvement has impacted the trial, we hope to help other trialists and advocates design future trials and clinical practices that are more patient-centric. In the introduction we discuss what we mean by patient-centric trials – trials that address issues important to patients and that are widely available, attractive, and easy to participate in by diverse patients. We also summarize the overall structure, goals, and evolution of the I-SPY2 trial which has been running for more than a decade with the goal of identifying potential improvements in care for patients with early-stage breast cancer that has a high risk of recurring. We then describe: 1) our philosophy of advocate involvement and the roles they play in I-SPY2; 2) specific attributes of the trial design that make it especially patient-centric; and 3) educational material and communications approaches aimed at empowering and supporting trial participants. For each section, in addition to describing I-SPY2 practices, we provide aspirational suggestions that could enhance I-SPY2 and/or other clinical trials. Embedding advocates into every aspect of clinical trial design and operations, empowering trial participants with excellent patient educational material, and incorporating and learning from patient-reported outcomes, serves as a model approach to achieve more patient-centric clinical trials.

OPEN ACCESS

Published: July 31, 2023

Citation: Perlmutter J, Brain S, et al., 2023. Advocate involvement in Clinical Trials: Lessons from the Patient-centric I-SPY2 Breast Cancer Trial, Medical Research Archives, [online] 11(6). https://doi.org/10.18103/mra.v11i7.2.4085

DOI
https://doi.org/10.18103/mra.v11i7.2.4085

ISSN: 2375-1924

INTRODUCTION

Well-designed, efficient clinical trials are one of the cornerstones of evidence-based medicine. They establish a scientific foundation for evaluating new approaches to the prevention, diagnosis, and treatment of disease. However, clinical trial design typically focuses on answering scientific hypotheses, with limited consideration of the needs and preferences of patients in general and trial participants in particular. This characteristic leads to several unintended deleterious effects including slow enrollment, high dropout rates and limited generalizability of study results. In an era where the cost of trials continues to increase and funding for academic trials is limited, incorporating patients' perspectives in the design of clinical trials becomes an opportunity to improve trial accrual and make them more cost effective and generalizable.

Over the course of the past 15 years, we have been part of the advocacy team of the I-SPY2 trial – an innovative, patient-centric clinical trial of new therapeutic strategies for early-stage breast cancer. In this paper, we describe how advocates have been embedded in the trial, giving voice to patients' perspectives and priorities, and making the trial more patient-centric from inception through to analysis and reporting. By describing the I-SPY2 example, we hope to help other trialists and advocates design future trials and clinical study practices that are more patient-centric.

In the introduction we define patient-centricity and briefly summarize the overall structure, goals, and evolution of the I-SPY2 trial. In the body of the paper, we describe: 1) our philosophy of advocate involvement and the roles they play in I-SPY2; 2) specific attributes of the trial design that make it especially patient-centric; and 3) educational material and communications approaches aimed at empowering and supporting trial participants. For each section, in addition to describing I-SPY2 practices, we provide aspirational suggestions that could enhance I-SPY2 and/or other clinical trials.

What is a Patient-Centric Trial?

As explained by PCORI, the Patient-centric Outcomes Research Institute, patient-centric research entails patient engagement that includes "active incorporation of perspectives beyond those of the researchers, to inform decisions about research questions, study design, measures used, practical aspects of study implementation particularly related to recruitment and data collection, data interpretation, and/or dissemination of results."[1] In other words, to establish a truly patient-centric clinical trial requires investigators to both understand and incorporate patients' needs and desires at virtually every level of trial design, implementation and operations. Patient-centric research is based upon the premise that the perspective of end-users of research – patients, physicians, and other stakeholders – establishes research that is more relevant to healthcare decisions faced by the end-user.[2] Simply put, patient-centric trials ask questions important to patients in a way that maximizes potential benefits, while minimizing burdens of participation.

What is the I-SPY2 Trial?

I-SPY2 is an innovative phase 2 response-adaptive, randomized clinical trial platform for patients with early-stage breast cancer that has a high risk of recurrence. Running for more than a decade, I-SPY2 was among the earliest platform trials, now the longest running, and widely regarded as the archetype of this advanced trial design.[3–5] Using a master protocol, it permits the evaluation of multiple investigational agents in parallel, allowing investigational agents to enter and leave the trial based on completion of maximum accrual, graduation, or futility, through protocol amendments and speeding the accumulation of new knowledge.[6]

I-SPY2 is designed to incrementally advance precision medicine, harmonize research and care, and develop innovative patient-centric design features. A precursor to I-SPY2, I-SPY1 was a multicenter non-treatment trial developed by the NCI Specialized Programs of Research Excellence (SPORE) designed to explore the use of MRI as a non-invasive assessment of treatment response, that was subsequently used for decision-making in I-SPY2. The latest iteration of the trial, I-SPY2.2 introduces several design features that not only more closely resemble clinical decision-making but respond directly to the needs of individual trial participants. Figure 1 shows the evolution of I-SPY. Many of the scientific findings from the trial have been summarized in more than fifty publications.[7] Here we focus on the roles of patient advocates and the impact they have had on the evolution of I-SPY2 towards increasing patient-centricity.

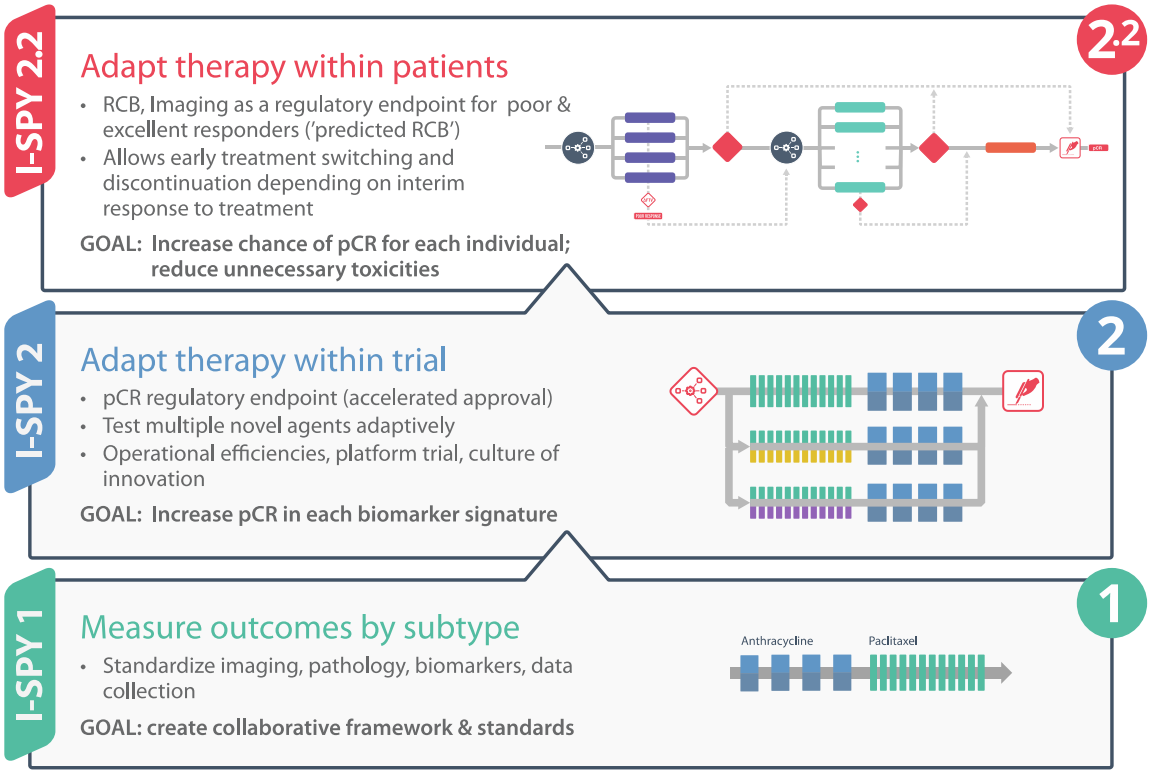

Figure 1: Evolution and increasing patient-centric approach of I-SPY2

I-SPY2 ADVOCACY

Fifteen years ago, an ambitious group of clinicians and scientists anticipated the new focus on patient-centricity in clinical trials by inviting advocates to participate in designing their new trial. For advocates at the time, it felt like an important opportunity -- embedded advocates as a foundational element of a strategy to promote more patient-centric trials [8]. Today, it has become clear to all stakeholders that advocates have helped shape I-SPY2 in ways that could not have been predicted when this journey began. Further, over the past 15 years advocates have increasingly become involved in a significant proportion of other cancer clinical trials.[9,10]

I-SPY2 advocates are former patients themselves, often former clinical trial participants. They bring a deep understanding of the patient and family experience regarding both their breast cancer diagnosis, and clinical trial participation. When advocates are involved in study planning, they help ensure the trial design and treatments are consistent with patients' needs and minimize the burden of participation during an emotionally difficult time. As trials accrue, advocates are also well equipped to recommend improvements that honor individual needs and preferences and clear the way to achieve the best possible outcomes. I-SPY2 advocates are trained and experienced in how to communicate the patients' perspectives successfully to investigators. Three principles that have guided effective advocate involvement in I-SPY2 are summarized below.[11]

Involvement Early and Often: For several years surrounding the opening of I-SPY2, advocates held webinars, organized forums at breast cancer conferences and sent email to hundreds of advocates to solicit input and buy-in and increase awareness among the survivor community about the trial. More than 200 advocates received regular updates and several dozens of them were and continue to be actively involved in I-SPY2 Working Groups (WGs) that establish scientific goals, set policy and procedures, and monitor progress of the many scientific and operational tasks in the trial. I-SPY2 internal WG focus on Study Design, Clinical Operations, Biomarkers, Imaging, Agent Selection, Pathology, Safety, Regulatory, Data Access and Publications, Patient Reported Outcome (PROs). External Advisory Groups include a Data Safety Monitoring Board as well as groups that approve policy and new agents. Advocates are included in all these groups and were also involved in early design discussions with potential funders, pharma partners, FDA, and IRBs to represent the patient point of view. Advocates are also involved in many public presentations and publications.

Diversity of Advocates: All I-SPY2 advocates are volunteers; not paid trial staff. This role allows them to speak freely and honestly and to make patients

their top priority. As members of diverse communities and geographies who are involved with many cancer advocacy organizations, they bring a heterogenous set of experiences, professional backgrounds, and bodies of knowledge to their role. A plurality of advocate voices ensures a broader perspective, as advocates often have different viewpoints, perspectives, and risk tolerance, and no one voice is sufficient to represent the broader population. Several of the I-SPY2 trial advocates also work one-on-one with patients and their families through peer support programs at their local cancer centers or through other national non-profit organizations. This enables them to bring current concerns and priorities from diverse patients to the investigators.

Continuous Learning: Effective research advocates possess a keen interest and feel responsible to keep abreast of relevant research as well as technical aspects of the trials to which they contribute.[11] Most I-SPY2 advocates have gone through formal training in research advocacy (e.g. NBCC Project LEAD,[12] AACR Scientist Survivor Program[13]), regularly participate in advocate educational programs (e.g. Susan G. Komen Foundation's Advocate in Science program,[14] Research Advocate Network's Advocate Institute[15]) and attend relevant scientific meetings. Many of the advocates also play advocacy roles in other research projects, clinical trial consortia, grant reviews or guidelines committees. In addition, monthly I-SPY2 advocate webinars include presentations by WG chairs and investigators, as well as opportunities for advocates to discuss among themselves their advocacy experiences in I-SPY2 and elsewhere, with the goal of improving the advocate experience and effectiveness. More experienced advocates have made it a priority to help novice advocates gain experience and confidence in contributing to clinical trials. This commitment is accomplished, in part, by pairing more experienced advocates with less experienced advocates in internal WG and encouraging informal mentoring.

Future Directions: The following are suggested practices that take advocate engagement even further.

- Increase diversity of advocates to more broadly represent patients of all ethnic, gender, socio-economic, and geographic backgrounds.
- Provide compensation for advocates to not only increases their status in a project, but also to facilitate involvement of more diverse advocates.
- Provide financial support for advocate to attend relevant professional meetings and learning opportunities.
- Develop metrics to evaluate the effectiveness of advocate activities toward the goal of continuous improvement.

PATIENT-CENTRIC TRIAL DESIGN FEATURES

The goals of I-SPY2 are to achieve pathological complete response (pCR) for the greatest number of patients, minimize toxicity, and maximize quality of life. The I-SPY2 culture places a premium on continuous learning. This includes improvement in trial operations but has also been a cornerstone of the design itself. In particular, the use of a response adaptive design allows subsequent trial participants to benefit from what was learned from earlier participants. Further, as discussed below, I-SPY2.2 now also enables adaptation of treatment for individual participants within the period of the trial to maximize outcomes and minimize toxicity.

I-SPY2 (3/2010 -- 6/2022)

Neoadjuvant Therapy: In 2010 the choice of neoadjuvant therapy (NAT), in which systemic treatments are administered prior to surgery, was not an obvious one. At the time I-SPY2 was planned, the standard-of-care for early-stage breast cancer was adjuvant (surgery first followed by chemotherapy or endocrine therapy). Use of NAT was primarily recommended for patients with large tumors, with the hope of reducing tumor volume and thereby limiting surgery to lumpectomy rather than mastectomy. But other advantages of NAT have with important implications for patients. Traditionally it has been assumed that treatment is best based on stage at diagnosis. However, it is now known that information about response to therapy is also informative. Adjuvant therapy compromises the ability to determine whether systemic therapy has been effective. For most cancer patients, the 'not knowing' can contribute to persistent anxiety that can last for years after treatment. Providing systemic therapy first provides an indication of whether the cancer responded to therapy. This not only informs subsequent healthcare decision-making about surgery, radiation, and longer-term systemic therapy, but also provides prognostic information that is typically welcomed by patients.[16,17]

Pathological Complete Response Endpoint: The endpoint in I-SPY2 is pathological complete response (pCR) which is defined as elimination of cancer in the breast and axillary lymph nodes. When I-SPY2 opened for enrollment, an FDA path for approval of new agents in the neoadjuvant setting of early-stage breast cancer using pCR as an endpoint was not available. However, in part due to evidence provided by I-SPY2 that patients who achieve a pCR are likely to have favorable prognoses regardless of treatment or disease sub-

type, the FDA initiated an accelerated approval pathway based on pCR in 2014. This allows investigational agents to reach patients more quickly.[18,19]

Clinical Development in Early-stage Breast Cancer: When I-SPY2 began it was rare for an investigational agent to be tested in early-stage cancer settings (i.e., in patients with potentially curable disease) without first having demonstrated their efficacy in patients with metastatic disease. Indeed, some considered the concept unethical.[20] I-SPY2 advocates were vocal proponents for study of investigational agents in patients who have a high likelihood of experiencing recurrence of their early-stage breast cancer. Such an approach can significantly decrease the time it takes for efficacious new treatments to reach patients who could be cured by them. Preventing metastasis saves lives, rather than simply extending them.[21]

Agent Selection: Another important feature of I-SPY2 is the process for selecting investigational agents. The Agents WG, which includes advocates, meets monthly to discuss potential promising investigational agents. Those of significant interest are assigned "chaperones" who conduct a comprehensive review of the relevant research and present their findings to the entire WG. If the agent is met with significant interest by the WG and approved by the external Investigational Agent Steering Committee, it is added to the trial when another arm is closed. In the agent selection process, advocates' views on the real or potential adverse effects of an agent can be decisive in the acceptance or rejection of an emerging agent.

Control Arms: While standard of care (SoC), rather than placebos are generally used as control arms in oncology trials, most patients who agree to participate in cancer clinical trials do so with the hope of achieving better outcomes than are typically achieved with SoC. Thus, trials that assign fewer participants to the control arm and more participants to the arms that include investigational agents are preferred by trial participants and routinely encouraged by advocates. As shown in Figure 1 I-SPY2, includes multiple investigational arms that provide SoC treatment plus an investigational agent. Each investigational arm is compared to a common SoC control arm. Under the principles of patient-centric design, the relative size of the control arm should be minimized. In I-SPY2 approximately 20% of participants are assigned to the SoC control arm compared to the more common 50%. This is accomplished not only because multiple experimental arms share a common control arm, but also because the trial uses a response-adaptive randomization design in which randomization probabilities are adjusted based on early trial results, favoring better treatments.[22]

Minimizing Interventional Procedures: In many cancer clinical trials participants undergo additional studies including blood draws, biopsies, and scans that are not part of SoC. The advocates in I-SPY2 serve an important role in helping keep the extra procedures to a minimum and force conversation about tradeoffs between nice to have and must have. The focus is on procedures that impact decision-making. I-SPY2 also endorses a culture of data sharing, a priority of most cancer advocates. As a result, tissue collected during I-SPY2 has contributed to many secondary studies and advanced progress in ways that remains uncommon among trials that include non-SoC biopsies.

Patient-Reported Outcomes/Quality of Life: Patient-Reported Outcomes (PROs) play an important role in promoting patient-centricity by assessing outcomes that consider the patients' perspectives which often differs from their clinicians.[23] PROs can then be used to guide treatment decisions and optimize patient outcomes and are increasingly being accepted for drug registration purposes.[24,25] In I-SPY2, trial participants complete electronic PRO and Quality of life (QoL) questionnaires before, during, and after I-SPY2 treatment to assess the adverse effects of treatment and their consequences. As with other aspects of the trial, advocates are active in evaluating PRO/QoL surveys and ensuring that they do not overburden trial participants. Also, an I-SPY2 advocate subcommittee is developing a brochure to educate patients on the purpose and benefits of PRO/QoL. Less formal questionnaires and interviews about the procedures and practices of the trial are used to solicit feedback from participants and ensure continuous learning and improvement. Participants themselves, are the best gauge of the participant experience and how the study is meeting their needs

I-SPY2.2 (7/2022 – present)

Leveraging data from more than 2,000 I-SPY2 participants yielded new knowledge and led to the evolution of the trial called I-SPY2.2 which began recruiting patients in the summer of 2022. As described below, I-SPY2.2 delivers further on the goal of optimizing treatment for each trial participant. Advocates continue to be active in all aspects of the study and are working to examine the feasibility of incorporating additional patient-centric improvements.

Response Predictive Subtypes: For many decades, breast cancers have been categorized and treated based on ER, PR, and HER2 biomarkers. With input from advocates, I-SPY2 included many exploratory

biomarkers. The biomarkers were aimed at improving categorization of breast cancers to provide more targeted treatments leading to more effective and less toxic treatment of patients. Based on data from I-SPY2, immune sensitivity, DNA repair deficiency, and luminal vs. basil attributes of tumors have been incorporated into five newly defined subtypes.[26] In I-SPY2.2 trial participants receive targeted investigational agents that are most likely to impact their cancer based on the newly defined subtypes. An IDE (FDA Investigational Device Exemption) has been filed with the FDA to validate the subtype classification in I-SPY2.2.

Sequential Multiple Assignment Randomized Trial Design: Most cancer patients receive a sequence of treatment, but most cancer clinical trials assess treatments one at a time. While such an approach is ideal for obtaining FDA approval of investigational drugs, it is ill-suited to identify ideal treatments for patients. Sequential Multiple Assignment Randomized Trial (SMART) Designs in contrast, assess treatment regimens by randomizing participants multiple times as they move through a sequence of treatments.[27] I-SPY2.2 participants are randomized to two different stages of treatment and can receive a third treatment if evaluation after the first two randomized treatments suggests that a pCR was not achieved.

Treatment Optimization Strategy: A goal of I-SPY2.2 is to learn how to optimize treatment for individual trial participants – to minimize exposure to treatments that are not effective and eliminate overtreatment of trial participants whose cancer is no longer detected. This goal, supported by advocates, is achieved in I-SPY2.2 by offering appropriate participants the option of *early treatment switching* when a treatment is not working or *early surgery* when a pCR is very likely. Based on I-SPY2 data, an algorithm was developed to predict which participants are likely to benefit from these strategies. Specifically, if functional MRI (fMRI) shows no tumor reduction after six-weeks of treatment, the treatment is unlikely to help but may cause toxicity. Therefore, participants that meet this criterion are offered the option of *early treatment switching*.

Ample evidence from I-SPY2 and other studies show that achieving a pCR after neoadjuvant therapy in early-stage breast cancer is highly likely to result in long-term distant-disease free survival, regardless of tumor sub-type or treatment.[28] Further, pCR can be predicted based on an fMRI after twelve weeks of treatment.[29,30] In I-SPY2.2, participants whose twelve-week fMRI show they likely achieved a pCR receive a breast biopsy. If the biopsy is negative, participants are offered the option of *early surgery*, foregoing additional systemic therapy. The algorithm for predicting pCR will regularly be assessed and improved, possibly incorporating ctDNA.[31,32] A small number of participants who are offered and choose *early surgery* may end up having some remaining cancer. They and their healthcare provider can then choose an appropriate adjuvant therapy.

Minimizing Toxicities/Side Effects: Adverse effects of therapy are often of greater concern for patients than trial investigators appreciate. Advocates play an important role in reminding investigators of the need to minimize such effects. Patients are especially concerned about late-occurring toxicities such as cardio-toxicity often associated with Adriamycin and Cyclophosphamide (AC). Also of concern are long lasting toxicities such as peripheral neuropathy, often associated with taxanes. Both of AC and taxanes are chemotherapies often used as SoC in early-stage breast cancer. Finding ways to eliminate these chemotherapies for patients who do not benefit from them has been an overarching aim of I-SPY2, a goal that is beginning to be achieved in I-SPY2.2 due to the sequential nature of treatments and the *Treatment Optimization Strategy* described above. Specifically, since the first treatment is always a non-chemotherapy-based treatment, individual trial participants who are likely to achieve a pCR with this treatment alone can go to *early surgery* and avoid SoC chemotherapy completely. On the other hand, trial participants who do receive SoC but do not appear to be benefiting from it can go to *early switching*, reducing the amount of SoC chemotherapy they receive and its toxicity.

Future Directions: The following are suggested practices that could interest trial participants and could be incorporated into I-SPY2 or other trial designs.

- Allow participants to receive some of their care locally.
- Provide treating clinicians and trial participants with individual and comparative PRO data during the visit at which it is collected.
- Dose drugs based on personalized pharmacokinetics—how an individual absorbs, distributes, metabolizes, and tolerates a particular drug.
- Include non-tumor-based biomarkers such as the microbiome and genetics, to predict response and prevent toxicities.
- Develop endpoints that balance both efficacy and toxicity.
- Use patient preference designs to allow data from patients who choose not to be randomized to contribute to learning.
- Further reduce trial eligibility requirements.

PATIENT EDUCATIONAL MATERIALS AND COMMUNICATIONS

Advocates have first-hand experience with diagnosis, treatment, and survivorship -- they understand the emotional state and needs of patients and provide key insights that inform communications with patients enrolled in or considering participation in a trial. Patients with breast cancer often feel that their diagnosis is a giant leap into the unknown. They may have little understanding of their disease or implications of their decisions, and they often lack agency and voice. However, they very quickly become aware of the need for high-quality medical care, a roadmap through the treatment process, and help with decision-making. While patients cannot control all aspects of their active treatment and survivorship, they can learn about their disease's challenges and opportunities, including the implications of test results. I-SPY2 encourages trial participants to partner with their care team to receive the best treatment for their breast cancer. Effective communication with participants – in terms of content, timing, tone, and method of delivery – plays a critical role in achieving patient recruitment, retention, and adherence targets, which can be a costly aspect of trial operations and is a well-known Achilles heel of many trials.[33] The complexity of I-SPY2 creates educational challenges for potential and enrolled participants. Throughout the trial, I-SPY2 engages and empowers patients to become their own best advocate. This goal is accomplished using an ever-growing collection of patient-focused communications developed in partnership with advocates.

Patient Website

Most patients are introduced to the idea of volunteering for the I-SPY2 trial by their health care providers who then lead them to additional information at www.ispypatient.org. The I-SPY2 patient website stands apart from the more technical site (www.ispytrials.org) designed for subject matter experts.[34] The patient website's development was led by advocates who prioritized website topics, guided a patient-friendly design, and wrote or reviewed the copy. A key priority is to guide newly diagnosed patients through the decision-making process regarding trial participation and as they progress through the trial. Information about clinical trials in general and I-SPY2 specifically is presented in plain language in a multi-layered approach, and each page includes an embedded NIH dictionary. Extensive and indexed FAQs enable patients to easily find answers to any question about I-SPY2. The website is transparent about costs of participation and offers suggestions and resources that help mitigate costs. One of the goals of the website is to serve as a guide about how patients can advocate for themselves. This is accomplished through prompts, downloadable resources, checklists, and suggested question lists. A collection of videos featuring previous trial participants, advocates, and researchers are available that educate patients about the trial, visually explain how the trial works, including a timeline of treatment/procedures, and shared decision-making points in the trial. Using plain language and visual analogies, these videos are not only educational, but enhance the informed consent process.

Patient Choice/Shared Decision-making

Key attributes of patient-centric clinical trials are patient choice and shared decision-making between the participant and their health care providers. While all trials provide participants the option to participate (or not) and to drop out at any time, I-SPY2 includes additional choice points.

Two-Stage Consent Process: I-SPY2 uses a two-stage informed consent process consisting of 'Screening Consent' and subsequent 'Treatment Consent' for those who are eligible and considering participation. This avoids overwhelming patients with information or burdening them with unnecessary tasks should they be ineligible for the trial. If after screening a patient is found to be eligible but decides that treatment in the trial is not for them, they are invited to join an observational, *Real World Evidence Group*, in which their outcomes are followed regardless of the treatment they decide upon. Furthermore, treatment consent occurs after randomization to one of several experimental arms, allowing patients the opportunity to discuss the treatment with their physician before agreeing to participate. Much time and effort have been devoted to ensuring that both consent forms were written in plain, accessible language and formatted to make information easily digestible, and a manageable length.

Return of Results: Many trial participants experience anxiety as they await the results of laboratory tests and are confused by the technical details of the results. I-SPY2 has adopted a formal and detailed Return of Results (RoR) process to manage the delivery and discussion of test results at predetermined timepoints according to principles recommended by the National Academy of Sciences.[35] To ensure that participants understand their results the process includes: 1) an investigator checklist; 2) timely delivery of an individualized RoR letter; 3) participant/provider meeting (in person or virtually) for shared decision-making that leverages the ROR letter; and 4) documentation that the RoR

commitment has been fulfilled. The standardized RoR letter includes the purpose of the test, the participant's results and their meaning, an outline of next steps, as well as answers to common questions participants may have.

Other Patient Support Materials

Several additional standard communication materials are available to all I-SPY2 participants.

Recruitment Brochure: A two-page visually attractive IRB-approved overview of the trial is available as a recruitment aid at all sites.

Drug Information Sheets: Participants in I-SPY2 receive multiple sequential treatments (two in I-SPY2 and one, two or three in I-SPY2.2); yet their treatment consent contains information about all of these before starting the first treatment. Drug Information Sheets (DISs) were developed to provide "just-in-time" review information about each new treatment. They are provided just prior to starting a new treatment and list the names of the drug the individual participant will receive, the drugs' mechanisms of action, and all known side effects. After reviewing the DIS, participants are given an opportunity to ask questions. This approach considers individual information needs, and ensures participants receive information as it is needed.

Participant Thank You Cards: Attractive thank you cards, signed by "the I-SPY2 advocates" are sent to participants after they complete surgery.

Future Directions

The following are additional ways to increase participant support, engagement, and empowerment.

- Integrate all participant specific information (e.g., participant calendar, PRO/QoL questionnaires, informed consent documents, DISs, individual RoR) into a convenient and secure participant web-portal with two-way investigator communication.
- Provide additional information about financial impacts of participating the trial and potential sources of financial support.
- Provide plain language aggregate summaries of the results of each study arm and other important I-SPY2 results.[36]
- Providing additional translation of the patient website, informed consent documents, and other participant-facing support material.
- Track the usage and value of each patient webpage and all participant-facing support material.
- Implement eConsent.

CONCLUSIONS

Research advocates are a valuable resource in the design and operation of clinical trials, because they provide a voice for the concerns, needs and priorities of patients in general and trial participants in particular. Patients with a new cancer diagnosis often feel that they are taking a giant leap into the unknown. They may have little understanding of their disease or the implications of their treatment decisions, and they often lack agency and voice. Advocates understand the physical and emotional states of the newly diagnosed, their expectations and their priorities. Most importantly, advocates are willing partners who are passionate about the development of better, more tolerable treatments and understand that improved participation in clinical trials depends on making clinical trials more patient-centric. Figure 2 summarizes our vision of how embedding advocates into every aspect of clinical trial design and operations, empowering trial participants with excellent patient educational material and incorporating and learning from patient-reported outcomes serves as a model approach to achieve more patient-centric clinical trials.

Conflicts of Interest: The authors have no potential conflicts of interest to disclose.

Funding Statement: All advocate authors are non-paid volunteers. The authors wish to acknowledge the generous support of the study sponsors, Quantum Leap Healthcare Collaborative (QLHC, 2013 to present) and the Foundation for the National Institutes of Health (2010 to 2012). The authors sincerely appreciate the ongoing support for the I-SPY2 Trial from the National Institutes of Health National Cancer Institute (grant P01CA210961), Safeway Foundation, the William K. Bowes, Jr. Foundation, Give Breast Cancer the Boot, QLHC and the Breast Cancer Research Foundation.

Acknowledgements: We are enormously appreciative to all the I-SPY2 investigators for their dedication to advancing the treatment of patients affected by breast cancer and their generous and collaborative involvement in this innovative trial; we especially appreciate their enthusiasm for partnering with advocates. The initial trial Principal Investigators (PI), Laura Esserman and Don Berry, deserve special recognition for the vision and fortitude they demonstrated as they pushed the envelope in the ways clinical trials are conceptualized to accelerate learning for future patients diagnosed with breast cancer. As sole PI, Laura's vision and commitment continue to evolve the trial and provide increasingly effective and individualized treatments for trial participants.

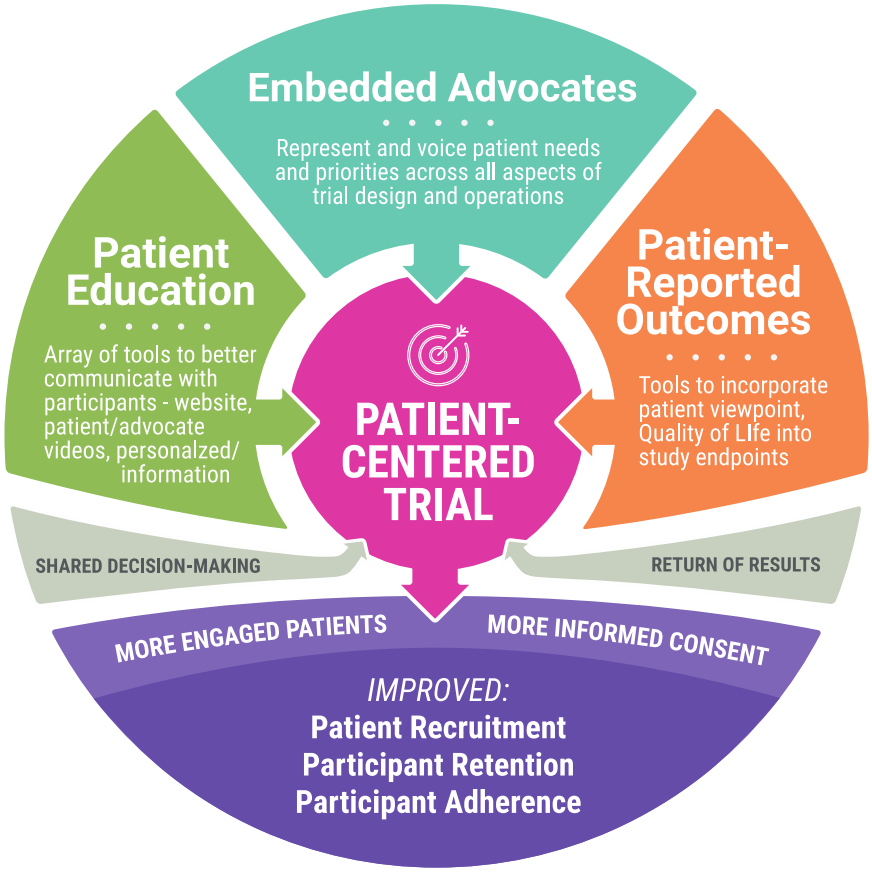

Figure 2: Embedded advocates are one of the key elements to creating patient-centered trials

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