Chapter 3 |

History of GOG Partners

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In 2010, the GOG Partners (GOG-P) program was formed under the umbrella of the GOG Foundation (GOG-F). The GOG-F is a corporate member of the NRG Oncology Inc. (NRG). GOG-P sits alongside the NRG Gynecologic Cancer Committee under the GOG-F organizational structure (Fig. 1). NRG was formed from the amalgamation of three legacy cooperative groups: the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG). As part of the National Cancer Institute (NCI) National Clinical Trials Network (NCTN), the NRG Gynecologic Cancer Committee is federally funded and is distinct from GOG-P, which functions outside of the NCTN framework without federal funding support. Through GOG-F's two investigative mechanisms (NRG-GOG and GOG-P), a rich portfolio of predominately therapeutic trials are conducted, although notable screening/prevention efforts have also been undertaken (e.g. GOG-0199: prospective study of risk-reducing salpingo-oophorectomy and longitudinal CA-125 screening among women at increased genetic risk of ovarian cancer).

GOG-P is structured to work directly with non-federally funded sponsors (e.g., pharmaceutical and medical device companies, philanthropic organizations) to coordinate clinical trials that fall outside of the NCI framework. By functioning as a site management organization (SMO), GOG-P provides an additional platform for patient accrual and site infrastructure support and significantly expands the national gynecologic oncology clinical trials network.

GOG-F and GOG- P have evolved organically through a series of retreats (Fig. 2). Today, GOG-P is led by a team of gynecologic cancer physicians, as well as operational and administrative teams. The Executive Leadership Committee of the GOG-P is comprised of the GOG-F President, Vice President(s), two physician Directors, two physician Associate Directors and GOG-F senior operational and administrative leads. Considering the Foundation's structure, physician members can serve in leadership roles of both organizations. Under the direction of the Executive Leadership Committee, there is a "G8" committee (initially this committee had eight members). In addition to the Directors and Associate Directors, the remainder of the G8 is comprised of additional physicians who serve as Clinical Trial Leads for one or more disease groups: 1) Uterine corpus cancer 2) Cervical and vulvar cancers, and 3) Ovarian, peritoneal, and tubal

cancers. The G8 committee members organizationally report to the GOG-F President and Vice-President.

Figure 1.

DEVELOPING AND LAUNCHING CLINICAL TRIALS

Fundamental to the continuing success of GOG-P is re-imagining processes to improve operational efficiency (Fig. 3). Clinical trial activation and completion requires successful navigation and continuous monitoring of several key factors. Key metrics such as the first site activated, first and last patient enrolled, site enrollment velocity, data quality, prevalence of disease and existing trial portfolio are among several variables captured in addition to study start-up. Parallel functions of study development and activation are outlined in seven steps (Fig. 3).

1. Initial Contact with Sponsor and Mutual Confidential Disclosure Agreement (CDA)

At every step in the development process, confidentiality and intellectual property protection is of the utmost importance. Typically, after execution of a Mutual CDA, the GOG–P teams conducts an introductory call that includes all relevant parties (e.g., key investigators, opinion leaders, sponsor, GOG-P staff and the G8 members). If the development plan is unclear, a scientific advisory board may be recommended. Additional key topics discussed early in development include the selection of a CRO, statistician, protocol writer, principal investigator, the possibility of international collaboration, and a lead group.

2. Overview of Early Operational Aspects of Trial

After the execution of the Mutual CDA, and the conduct of the introductory call, a Letter of Authorization (LOA) is negotiated and executed with the company. Execution of the LOA allows the GOG-P team to begin start-up activities. The study is assigned a GOG-P protocol number, and then site interest, execution of site CDAs, feasibility, and site selection begins. No U.S. sites outside of the GOG-F network will be involved in the trial, but new sites interested in participation are vetted expeditiously by the GOG-F to become a participating institution. Additional startup activities include the conduct of budget negotiations between the GOG-F and the sponsor for the overall clinical trial budget and the site budget. Finally, standing operational calls that include GOG-P staff, G8 physicians, sponsor and CRO members occur throughout study start-up, study development and enrollment.

2.1 Letter of Authorization (LOA)

As mentioned above, execution of the LOA is a critical step because it allows the GOG-P team to begin work on the project. The LOA includes a retainer to cover the work hours expended by the GOG-P team in performing the startup activities. The LOA is a bridge to the Clinical Trial Services Agreement (CTSA).

2.2 Responsible, Accountable, Consulting and Informed (RACI) Table

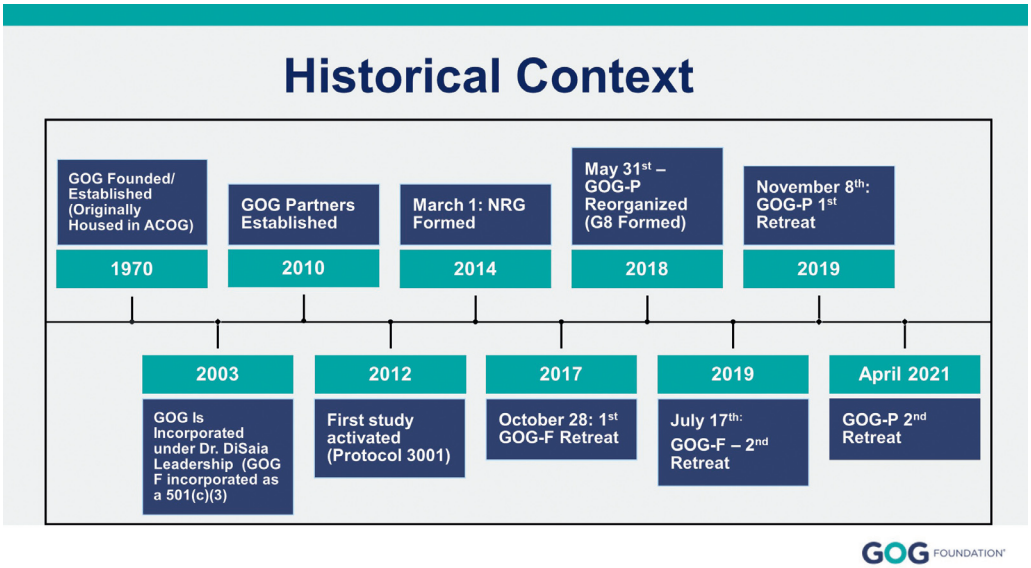
Under the LOA, and in addition to early operational aspects outlined above, a RACI Table is negotiated. This matrix defines the roles and responsibilities of all parties such as GOG-P, CRO and sponsor. During this phase, the protocol is also finalized. Regulatory processes, such as the US Food and Drug Administration (FDA) meetings, are planned. The GOG-P is also prepared to participate in scientific review and help coordinate IRB submissions. The services delineated in the RACI provide a component for the final overall study budget.

2.3 Clinical Trial Services Agreement (CTSA) and Site CTA Template

In parallel to the conduct of the startup activities, the CTSA is negotiated with the sponsor with the goal of execution after all of the above activities are completed. As part of the CTSA negotiations, the Site CTA template also is negotiated with the sponsor. The GOG-F has in-house legal counsel to expedite all contract negotiations. Ex-

hibits to the CTSA include the final study budget, including the site budget, the final Site CTA template, and the final RACI. The high-level items (statistical and data plan, Trial Steering Committee [TSC] related activities, publication rules, Independent Data Safety Monitoring Committee [IDMC], biomarker procurement/analysis and imaging charters) may be covered in the CTSA.

Figure 2.



2.4 Site Clinical Trial Agreement (CTA)

Being a SMO, site engagement is key. Efficient communication is foundational. The Site CTA template is negotiated between the GOG-F and the sponsor in parallel to the startup activities. The GOG-F team maintains excellent communications with the investigators and the staff at the participating institutions. After execution of the CTSA, the Site CTAs, including the site budget, are released to the selected participating sites. Site Prequalification Visits (SPV), followed by Site Initiation Visits (SIV) and group-wide Investigator Meeting are scheduled by Sponsor and CRO.

GOG-P COMMITTEES

The GOG-P structure provides other key opportunities to promote scientific engagement and discovery, as new treatments and strategies are brought to women with gynecologic cancers. Many of these tasks are coordinated through six committees. In addition to its function as a SMO, the GOG-P program includes the GOG-P Publications Committee, and a group of key committed investigators that function as the Investigator Council.

International Relations Committee

In light of its domestic footprint in clinical trial governance and core mission, GOG-F leadership collaborates with other gynecologic cancer research organizations and groups throughout the world to broadly address the needs of our patients in the global community. In particular, collaborative guidelines are now in place with the Gynecologic Cancer Intergroup (GCIG) and the European Network of Gynecological Oncological Trial Groups (ENGOT), Canada and Latin American Cooperative Oncology Group (LACOG). These relationships are coordinated by the GOG-F International Relations Committee and a sub-committee, the ENGOT/GOG Liaison Committee.

Development Committee

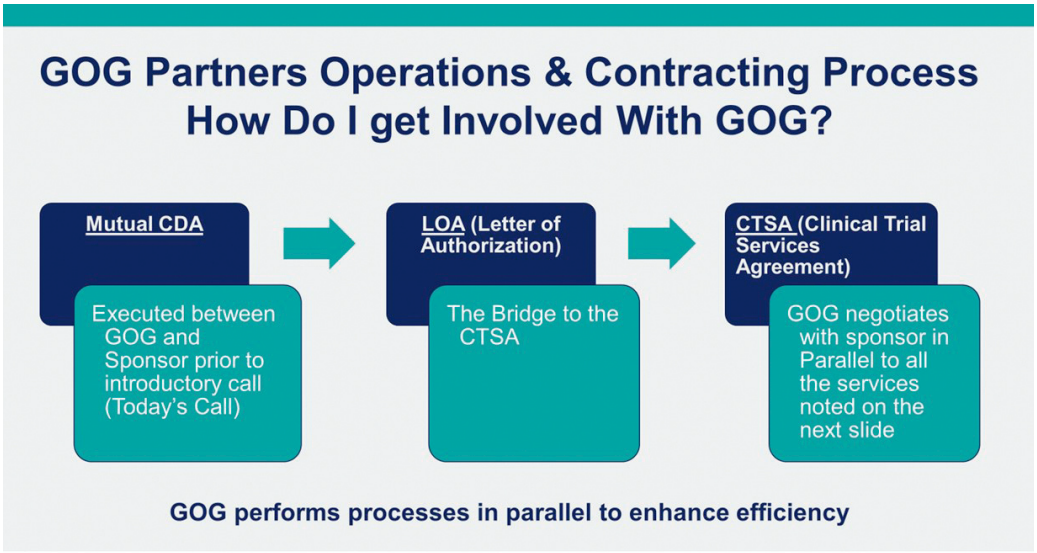
To promote and expand relationships with investigators, sponsors, and other key stakeholders, a committee has been created to coordinate this effort. The four main functions of the committee include:

1) Philanthropy: Expand and promote philanthropic support from individuals and groups who are interested in contributing to gynecologic oncology research.

2) Industry Collaboration Team (ICT): The GOG-F offers membership into an ICT (See Supplementary Appendix B). This is a yearly GOG-F membership program for industry designed and developed to foster and facilitate communication between parties. Membership in the ICT creates multiple key opportunities including reduced meeting registration fees, and complimentary tabletop exhibit space at two semiannual meetings. These meetings include over 1500 attendees. Most of the attendees are gynecologic oncologists, surgical oncologists, radiation oncologists, pathologists and medical oncologists who diagnose and treat gynecologic cancers.

3) Advisory Boards: The GOG-F maintains staff tasked with the successful, efficient and timely performance of advisory opportunities with key opinion leaders that are recommended at key decision points to maximize the chance of technical success (regulatory approval) as interventions are brought from the laboratory to the “bedside.” The GOG-F is equipped

Figure 3.



to coordinate in-person as well as virtual advisory forums with domestic and international advisors. The GOG-F team can provide all aspects of meeting planning including coordination of confidentiality agreements, contracting, as well as "Centers for Medicare & Medicaid Services (CMS) Open Payment" reporting [6].

4) Education: As emerging concepts evolve, including development of new therapeutic agents and advances in science, education becomes critical. Based on its relationships and footprint, the GOG-P provides opportunities and platforms to teach providers, payors and survivors.

Mentoring Committee

GOG-F is committed to training and mentoring the "next generation" of investigators and leaders. In this manner, GOG-F supports two types of awards: (1) GOG-F New Investigator Award, and (2) the GOG-F Scholar Investigator Award. The GOG-F New Investigator Award is a three-year award to identify new investigators with interests in clinical trials in gynecologic cancers who wish to become more engaged with GOG-F and to learn more about the gynecologic cancer clinical trial development process. It is anticipated that some new investigators might pursue a GOG-F Scholar Investigator Award at the time of future requests for applications of that award (a list of the 2019 recipients is in Supplementary Appendix C). Awardees are provided monetary support to attend meetings and gain access to other key educational opportunities.

The GOG-F Scholar Investigator Award is a five-year award aimed to identify, enhance, and support training for investigators who will be capable and committed to developing, executing, and leading gynecologic oncology clinical trials, conducting high-quality research related to gynecologic cancer, and participating in GOG-F and other relevant committee/leadership positions. This award funds investigators, who have academic or non-academic appointments, as they work to establish an independent clinical cancer research career with a patient-oriented clinical trial research focus in gynecologic cancer within the GOG-F. The applicants are required to present their research interest(s) and competencies as well as prior clinical trial research training. A five-year commitment at a minimum of 10% effort for GOG-F related gynecologic cancer clinical trial development activities is expected. A specific mentor is identified and supported. Annual progress reports are required, and continued support of the award is based upon extent to which obligations were made in the prior year.

Communications Committee

Engagement of all key stakeholders including, but not limited to, industry sponsors, NCI, investigators, cancer survivors and advocates is critical to the success of GOG-F clinical trials. Outlets are diverse and include coordinated messaging via social media, newsletters, press media, websites, face-to-face and virtual meetings. Strategic deliverables and opportunities are coordinated by the Communications Committee.

Quality and Assessment Committee

The coordination of quality assessments of sites and study data as well as ensuring compliance in all research areas is the responsibility of the Quality and Assessment Committee. Institutions and private practices interested in participating on GOG-P studies complete applications for review and approval by this committee.

Investigator Council

The purpose of the Investigator Council is to convene a group of investigators who have demonstrated a commitment to GOG-P studies by strong accrual and advocacy.

The establishment of this Council enables a supportive advisory role not only to GOG-P but also to sponsors – effectively extending opportunities and reach into the clinical investigative landscape. The mission of this Council will be actualized through fostering increased engagement and a culture of inclusivity amongst leaders at GOG-P sites, increasing our impact on pharmaceutical company decisions (via advisory boards and steering committee membership) regarding clinical trial design, interpretation, publication and regulatory opportunities. In addition, the GOG-F strives to promote network-wide best practices via increased site efficiency, speed, compliance and capacity as well as improve site training and education, and creating a culture of research in gynecologic cancers beyond our existing participating sites.

Fundamental to the continuing success of GOG-P is re-imagining processes to improve operational efficiency (Figure 2). Clinical trial activation and completion requires successful navigation and continuous monitoring of several key factors. Key metrics such as the first site activated, first and last patient enrolled, site enrollment velocity, data quality, prevalence of disease and existing trial portfolio are among several variables captured in addition to study startup. Parallel functions of study development and activation are outlined in several steps.

Operationalizing a sustainable roadmap for GOG-P comes with the customary challenges of any business, including development, managing resources and expenses, and innovation. In addition, given the legacy of the "Gynecologic Oncology Group" nomenclature, confusion over the current structure of GOG-P, its focus, and its function, is a prevalent challenge and was a key motivator for this manuscript. Additional education is currently available through a newly rebuilt website (gog.org). Another key component of sustainability is demonstrating value to potential industry sponsors. Value can be tricky to quantify but given the competitive nature of clinical investigation, temporal metrics (e.g., time to first site open, time to first patient in, time to last patient in), data quality, and successful new drug applications are key strategic variables. In addition, comprehensive knowledge of the contractual processes for GOG-P participating sites provides a structural enhancement to CROs and sponsors in developing expectations. Integrated technology solutions are thus necessary to provide accurate and real-time data, particularly for site feasibility, site engagement, and enrollment rate. The latter is usually represented as patients per site per month and can vary widely depending on eligibility parameters and prevalence. However, this metric is key to developing necessary number of sites under a sponsor's desired completion time. Ultimately, as the GOG-P portfolio grows, broader use of the potential sites within the network will be a desired development. Finally, as alluded to earlier, development of the next generation of clinical trialists is key to GOG-P's sustainability. Continued development and investment of the investigator's council and the mentored investigator program will be necessary to meet GOG-P's aspirational goals.

The goals of the GOG-P include the development of diagnostics, surgical devices, novel therapeutics, and clinical pathways, while bringing value to stakeholders. Enhancing the patient experience is also an important goal. Working with sponsors, investigators, patients, survivors, advocates and regulators, the GOG-F has evolved GOG-P into the premier organization to mentor investigators and bring revolutionary new opportunities to clinical gynecologic oncology.