The Trial-Ready Clinician: Integrating Research into Standard Patient Care- The Experience of Gynecologic Oncology

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Baystate Health

Disclosures

Consultant GSK, AbbVie, Gilead Science (Tashanna Myers)

None (Laura Sorci)

Qualifications and Disclaimers

- 17 years at Baystate Health
- PI on >80 IRBNET submissions
- >10 Years as leading enroller for gynecologic oncology trials nationally
- Many mistakes made, more lessons learned

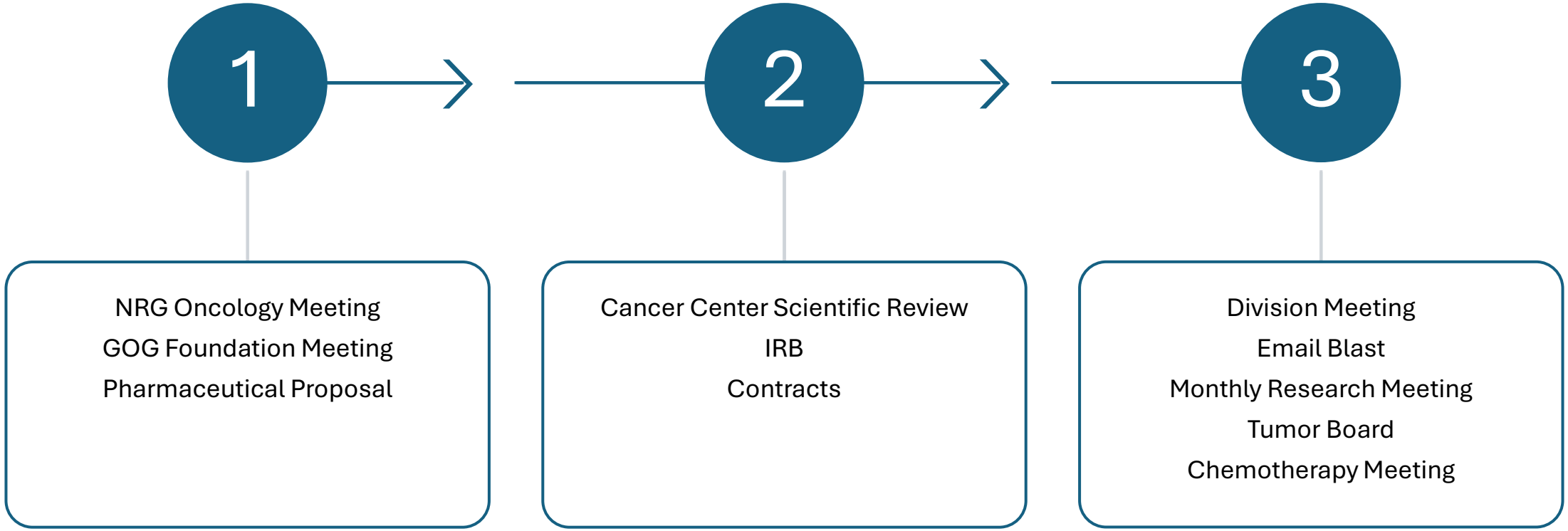
Objectives

- Describe the operations of clinical trial management of Gynecologic Oncology @ Baystate Health
- Describe tools to integrate research into a busy clinical practice
- Review key research leadership strategies

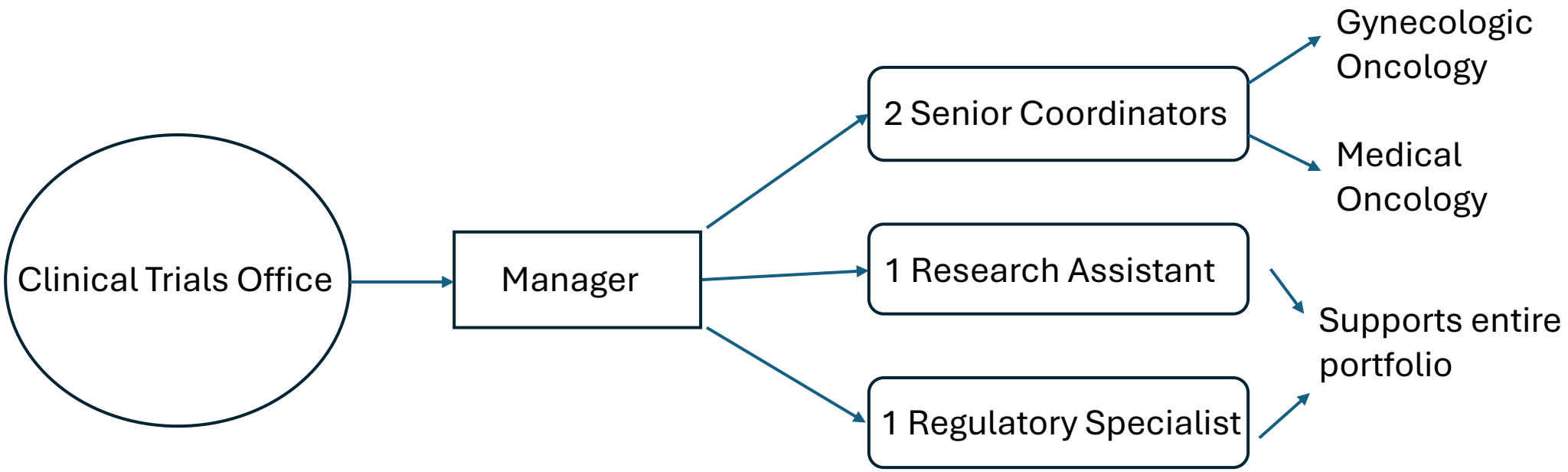
Team

Physicians	Oncology CTO	Nurses	Patients
PI- Tashanna Myers, Sub –I- Lindsay West, MD Sub I , Erica Weston, MD Sub-I Sarah Irish, DNP	Laura Sorci Jennifer Blanquart Theresa Hall Ally McDonald Katie Colbeck	Tirena Jackson, RN Jeanne Gagliarducci, RN (CTO)	Division of Gynecologic Oncology (focused practice)

Gyn Cancer Research Algorithm



Cancer Services Research Team



This team manages the **operational side** of opening, execution of the trial, data entry and regulatory compliance.

Cancer Scientific Review Committee Members

- Physician Representation from all the disease sites (Heme, GI, GU, Lung, Melanoma, Breast, GYN, Pediatrics)
- Physician Representation Radiation Oncology
- Oncology Nursing Outpatient Infusion Suite
- CTO Team Members
- Pharmacy

Scientific Review Committee

- A proposed protocol is sent to the Cancer SRC
- The SRC will review whether the study is feasible given the available resources, staffing, budget, protocol required assessments and patient population.
- A study is allowed to move forward only after all concerns have been addressed, and a majority of members have given their approval.

CTO Operations

- Continuously evolves based on volume and staff.
- **CTO Weekly meetings**
  - discuss the number of active/follow-up patients
  - assess workload to evaluate staffing distribution.
- Regular and frequent **communication** with our physicians regarding study progress, portfolio gaps or lagging enrollment

Monthly CTO-Gyn Oncology Meetings

- Portfolio Review by Disease Site
- Enrollment
- In the pipeline
- Screening Activity

Ovarian Studies

CC008 Risk Reduction

- BLS or BSO +/- Hysterectomy
- **Accrual: 1153/1956, BMC 10**

DS6000-109: High grade serous or endometrioid PROC

- R-DXd vs Investigator's Choice (PLD, Paclitaxel, Topotecan)
- **Accrual: 503/660, BMC 0**

GY036: First Line Maintenance BRCA or HRD positive OC

- Olaparib 300mg BID for 2 yrs vs 1 yr +/- Bev
- **Accrual: 338/880, BMC 2**

ZN-c3-005: High Grade Serous PROC

- ZN-c3 PO
- **Accrual goal: 140, BMC 3**

Endometrial Studies

GY026 - Primary Stage I-IVB, All Her2+ histologies

- Arm 1 Carbo/Taxol q 3wks x 6 cycles
- Arm 2 Carbo/Taxol/Herceptin Hylecta q 3wks x 6 cycles + Maintenance Herceptin Hylecta
- Arm 3 Carbo/Taxol/Pertuzumab/Phesgo q 3 wks. x 6 cycles + Maintenance Phesgo
- **Accrual: 349/360, BMC 2**

GY032 – Early Stage Tailored Adjuvant Therapy

- Stage IA, IB or II POLE-mutated or P53wt/NSMP
- **Accrual: 73/395, BMC 2**

Vulvar

GY024

Primary T1 tumors: replacing IFL with chemo RT

- Concurrent CIS/RT over 5-6 weeks
  - ➢Accrual 27/202, BMC 2

Cervix

GY037 - High risk locally advanced with or without lymph node involvement

- CCRT + pembro vs carbo/Taxol + CCRT + pembro

➢ Accrual 84/336, BMC 0

Studies in Pipeline

Endometrial				
Study	Phase/Disease	Treatment	Eligibility	Status
GOG-3131	III (open label) – recurrent EC	IP vs choice of Taxol or doxorubicin	1-2 prior lines including platinum based and PD-1	ICF with legal for injury language review
GOG-3145	III (open label)- Stage III/IV or recurrent EC	IP + chemo vs pembro +chemo	pMMR	FQ submitted – waiting for site selection
Ovarian				
GOG-3136	III (open label) - PSOC	IP +Bev vs SOC +Bev	HGS or HGE 1-2 prior lines	Working on IRB submission
GOG-3146	III (Double blind) – Stage III/IV 1L Manit OC	IP +Bev vs placebo Bev	HGS/HGE/CC Cyclin E1 Not eligible for PARP	Study documents received Going to Scientific Review
GOG-3138	III (open label) –2L Maint PSOC	IP +/- Bev vs SOC	HGS or HGE Must have received 2 prior lines of platinum	Study documents received Going to Scientific Review

Year-to-Date Enrollment

Study	Dr. Myers	Dr. West	Dr. Weston
CC008	2		
GY024			
GY026			
GY032			1
GY036	2		
GY037			
ZN	1		
Total	**5**		**1**

NRG (GYN): 5
GOG Partners:1
NRG (Breast): 2 (Dr. Sakr)

NRG Accrual Credit: 8/10

Ouch ! Accountability

Change in eligibility for DS6000-109:

Subjects with 1-2 prior lines of therapy – must meet one of the following

- Received prior pembrolizumab in combination with paclitaxel +/- bevacizumab
- Received prior relacorilant in combination with nab-paclitaxel
- Either PD-L1 CPS < 1 or any prior anti-PD-1/PD-L1 treatment and contraindication to relacorilant and nab-paclitaxel
- Has documented active Grade 2 peripheral neuropathy

Subjects with 3 prior lines of therapy – must meet one of the following

- Received prior pembrolizumab in combination with paclitaxel +/- bevacizumab
- Received prior relacorilant in combination with nab-paclitaxel
- Contraindication to relacorilant and nab-paclitaxel
- Has documented active Grade 2 peripheral neuropathy

Potential Patients

Dr. Myers:

ZN

- 1 patient pending pre-screening consent
- 1 patient positive for cyclin and waiting for progression

Dr. Weston

- 2 potentials for CC008 (one seeing West in October and one seeing Myers in December)

Dr. West

Office Integration



Baystate Health

OFFICE RESEARCH FLOWCHARTS

Ovarian Cancer

First Line Maintenance

GY036

- Stage III/IV HGS, high grade endometrioid, or other epithelial ovarian cancer
- BRCA 1/2 variant or BRCA 1/2 wildtype with known HRD deficiency
- Primary or interval surgery required
- Completion of 4-9 cycles of platinum-based chemo with PR or CR response

Rx: Olaparib 300mg BID for 2 years vs. one year (+/- bevacizumab physician's choice). (1:1)

Recurrent PROC High Grade Serous

ZN-c3-005

- Cyclin E1 positive tumors only (pre-screened)
- No platinum refractory
- 1-3 prior lines allowed (4 priors allowed if received MIRV)
- Prior PARP, prior bev and prior MIRV (if FRα high) required if no contraindication
- At least 1 measurable lesion by RECIST

Rx: ZN-c3 PO (one cycle q 21 days)

Recurrent PROC High Grade Serous or Endometrioid

DS6000

- 1-3 prior lines allowed
- Prior PARP (if BRCA +), prior bev and prior MIRV (if FRα high) required if no contraindication
- No sarcomatous or mixed tumor histology
- At least 1 measurable lesion by RECIST

Rx: R-DXd (CDH6 ADC) vs Investigator's Choice PLD, topotecan, paclitaxel (1:1)

Risk Reduction

CC008

- BRCA 1 carriers ages 35-50
- Pre-menopausal or menopausal
- TVUS and CA125 within 180 days of registration

Surgery: Bilateral salpingectomy or Bilateral Salpingo-oophorectomy +/- hysterectomy

Cervical Cancer

High Risk Locally Advanced

GY037

- T3 or T4 with or without lymph node involvement
- No prior hysterectomy or plan for hysterectomy as part of initial therapy
- No paraaortic lymph node metastases above the T12/L1 interspace

Rx: CCRT + pembro vs carbo/taxol + CCRT + Pembro

Endometrial Cancer

Stage I-II Tailored Adjuvant Therapy

GY032

- POLE mutated: Stage I-II endometrioid, serous, clear cell, un/dedifferentiated, carcinosarcoma or mixed
- P53wt/NSMP: Stage I-II endometrioid only, ER positive
- No macroscopic residual disease after surgery, no positive surgical margins, no positive peritoneal washing
- P53wt/NSMP with a MELF pattern are not eligible
- Focal definition (< 3 foci), substantial (≥ 3 foci)

Rx: See chart below

Eligible Groups – by stage and molecular subtype	**Protocol Adjuvant treatment**	
	POLE-mutated	**P53wt/NSMP**
Histotype	**Endometrioid, serous, clear cell, un-/dedifferentiated, carcinosarcoma, mixed**	**Endometrioid only, ER positive**
• Stage IB, grade 1 or 2, pNx/N0, with no LVI or with focal LVI	Group A1.1 Observation	Group B1 Observation
• Stage IA (not confined to polyp), grade 3, pN0, with no LVI or with focal LVI • Stage IB, grade 3, pN0, with no LVI or with focal LVI • Stage II (microscopic), grade 1 or 2, pN0, with no LVI or with focal LVI	Group A1.2 Observation	Group B2 Vaginal brachytherapy
• Stage IA (not confined to polyp), grade 3, pN0, with substantial/extensive LVI • Stage IB, grade 1 or 2, pNx/N0, with substantial/extensive LVI	Group A1.3 Observation	

Vulvar Cancer

Primary Treatment – Replacing inguinofemoral lymphadenectomy by chemoradiation

GY024 – GROINSS

- T1 squamous cell carcinoma, tumor not encroaching urethra/vagina/anus
- Depth of invasion >1mm, tumor diameter < 4cm, unifocal tumor
- No enlarged (>1.5cm) or suspicious inguinofemoral lymph nodes on imaging
- Metastatic sentinel node >2mm and/or extracapsular extension, or more than 1 SN ≤ 2mm

Rx: Concurrent Cis/RT over 5-6 weeks

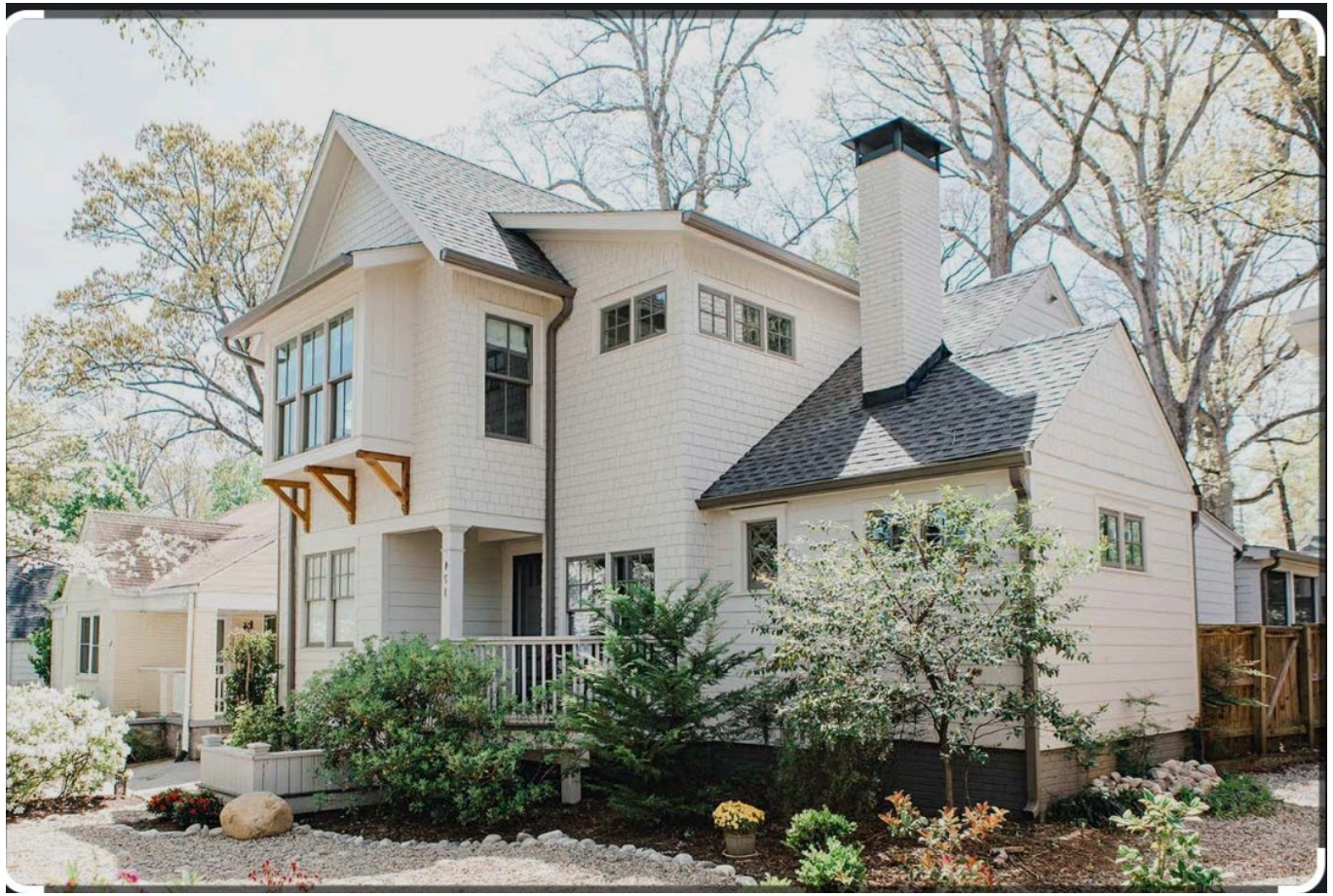
Details of Integration

- Office Flowcharts- Visual reminders
- Editor role to Outlook Calendar (Monitor /Site visits scheduling ease)
- Scheduled Monthly Meeting (Dedicated time)
- Weekly touch base (Operations)
- Invitation to team retreats, weekly tumor board, chemotherapy bi monthly meeting.

Does your research look/feel like this?



Or does it look like ...



A Day in the Life- Case Study

- SJ is referred for an abnormal CT from the emergency room. Presenting for consultation
  - In discussing standard of care I explain that following surgery she will be screened for clinical trials, have genetic testing and molecular profiling of her tumor. I offer participation in our tumor banking trial
- First post-op visit, I review the SOC treatment and clinical trial options.
- In review of the genetics and molecular profile, I discuss how this information can be used to identify trial options in the future.

A different Day in the life- Case Study

- SR had a diagnosis of endometrial cancer and surveillance CT shows a new lung nodule.
  - As the CT is reviewed, we discuss the need for biopsy - the possible need for treatment with SOC versus a clinical trial. I explain that we will be looking for those options to present once the biopsy is complete.
  - She appears to be eligible for a clinical trial by CRA screen.
  - I notify the patient via portal she is a candidate for trial ABC. I send the details and offer to send the consent for her to review.
  - I explain the value of a second opinion. It builds a greater confidence in the first recommendation and access to future clinical trials
  - Pathology returns recurrent disease- we meet in person to review the previous discussed trial and SOC. The CRA is present with a clean version and ICF is signed.

Research Integration

- Screening is for everyone – RN, CRA, Doctors and NPs
- Division Meetings discuss research,
  - Highlight compliance with vital signs being complete, Visits and imaging being ordered on schedule
  - Results of the study shared
- Each faculty is given their research numbers- accountability
- The nurses also advocate for research opportunities for patients

Challenges of Building a Research Team

Challenge	Strategy
• Building Trust as a PI	Listen/support the team concerns Facilitate open communication Be trustworthy
• Respect/understand the value of each team member	Every team member understands the goal/ expertise /value of the other team members
• Build investment/enthusiasm	Create a vision/mission Celebrate Team achievements
• Recognize high achievers	Advocate for team members Support their growth/promotion opportunities

Makris UE, Ferrante LE, Mody L. Leadership Lessons: Building and Nurturing a High-Performing Clinical Research Team. *J Am Geriatr Soc*. 2018;66(7):1258-1261. doi:10.1111/jgs.15352

Mission Statement

- Eradicate gynecologic cancer through evidence based clinical trials
- Elevate the care of women with gynecologic cancer in Western Massachusetts



- Brooks S, Carter R, Plaxe S …
- **Patient and physician factors associated with participation in cervical and uterine cancer trials: An NRG/GOG247 study**
- Gynecologic Oncology, 2015; 138, 101-108

Closing thoughts

Marie Curie, the Nobel Prize-winning physicist and chemist, offered:

"We must have perseverance and above all confidence in ourselves. We must believe that we are gifted for something and that this thing must be attained."