Highlights from the NCORP Committees

Prevention and Epidemiology

Co-chairs: Marian Neuhouser, Banu Arun

Survivorship

Co-chair: Robert Krouse

Katherine Crew, MD, MS

October 13, 2017

Outline

- **Prevention and Epidemiology**
  - S0701: Trial of three antibiotic regimens to eradicate *Helicobacter pylori*
  - S0812: High dose vitamin D in premenopausal women at high-risk for breast cancer
  - S0820: Preventing Adenomas of the Colon with Elfornithine and Sulindac (PACES)
- **Survivorship**
  - S0230: Prevention of Early Menopause Study (POEMS)
  - S1501: Carvedilol to prevent cardiac toxicity in patients with metastatic HER2+ breast cancer

14-day triple, 5-day concomitant, and 10-day sequential therapies for *Helicobacter pylori* infection in seven Latin American sites: a randomised trial

www.thelancet.com Vol 378 August 6, 2011

E Robert Greenberg, Garnet L Anderson, Douglas R Morgan, Javier Torres, William D Chey, Luis Eduardo Bravo, Ricardo L Dominguez, Catterina Ferreccio, Rolando Herrero, Eduardo C Lazcano-Ponce, María Mercedes Meza-Montenegro, Rodolfo Peña, Edgar M Peña, Eduardo Salazar-Martínez, Pelayo Correa, María Elena Martínez, Manuel Valdivieso, Gary E Goodman, John J Crowley, Laurence H Baker

- Promoting cancer prevention and control in low to middle income countries through the SWOG Latin America Initiative
- *Helicobacter pylori* infection accounts for the majority of gastric cancer cases.
- Gastric cancer is the second leading cause of cancer-related death worldwide, particularly in Latin America and East Asia.
- Population-wide eradication programs that are practical and affordable may reduce the health burden of *H.pylori* infection.

S0701: Study Design

- **Study population**: Healthy men and women, age 21-65, positive urea breath test for *H.pylori (N=1469)*
- **Study intervention:** 1) Standard triple therapy x14d (lansoprazole/amoxicillin/clarithromycin); 2) Concomitant therapy x 5d (lansoprazole/amoxicillin/clarithromycin/metronidazole); 3) Sequential therapy (lansoprazole/amoxicillin x5d, lansoprazole/ clarithromycin/metronidazole x5d)
- **Primary endpoint:** Eradication of *H.pylori* at 6-8wks

S0701: Results

	N	*Helicobacter pylori* eradication	Difference from standard group (adjusted 95% CI for difference)
Intention to treat (N= 1463)			
14-day standard therapy	488	401 (82·2% [78·5 to 85·5])	..
5-day concomitant therapy	489	360 (73·6% [69·5 to 77·5])	8·6% (2·6 to 14·5)
10-day sequential therapy	486	372 (76·5% [72·5 to 80·2])	5·6% (–0·4 to 11·6)
Definitive 6-week UBT (N=1414)			
14-day standard therapy	475	401 (84·4% [80·8 to 87·6])	..
5-day concomitant therapy	471	360 (76·4% [72·3 to 80·2])	8·0% (2·2 to 13·7)
10-day sequential therapy	468	372 (79·4% [75·5 to 83·1])	4·9% (–0·9 to 10·8)
Adherent to therapy (N=1314)			
14-day standard therapy	434	378 (87·1% [83·6 to 90·1])	..
5-day concomitant therapy	442	348 (78·7% [74·6 to 82·5])	8·4% (2·7 to 14·0)
10-day sequential therapy	438	355 (81·1% [77·1 to 84·6])	6·0% (0·3 to 11·8)

Data are number (% [95% CI]) unless otherwise indicated. UBT=urea breath test.

S0701: Conclusions

- The prevalence of *H.pylori* infection was high at ~80% in these Latin American sites.
- Compliance to all three antibiotic regimens was high at >90%.
- *H.pylori* eradication rates: 1) 14d standard therapy (82%), 2) 5d concomitant therapy (74%), 3) 10d sequential therapy (77%)
- *H.pylori* eradication programs may be cost-effective if they reduce peptic ulcer disease and prevent at least 10% of gastric cancer deaths.

SWOG Latin America Initiative

Risk of Recurrent *Helicobacter pylori* Infection 1 Year After Initial Eradication Therapy in 7 Latin American Communities

JAMA, February 13, 2013—Vol 309, No. 6

- **S1119**: Gastric cancer and *Helicobacter pylori* infection in Lima, Peru – Role of water contamination

- **Project STOP** (SWOG Tobacco program for the Oncology Practice): Development of eHealth/mHealth technology for cancer care providers to promote tobacco cessation in Brazil, Chile, and Peru *(SWOG/Hope Impact Awardee: Irene Tami-Maury)*

S0812, S0820: Early phase chemoprevention trials

- Large-scale chemoprevention trials with cancer incidence as the primary outcome require large sample sizes and long-term follow-up.
- Need for surrogate endpoints for cancer incidence in order to conduct more efficient chemoprevention trials.
- Translational potential with the analysis of tissue and circulating biomarkers of cancer risk to understand underlying mechanisms of carcinogenesis.

Knowledge gaps in breast cancer chemoprevention

- Need for safe and effective chemopreventive agents, particularly for high-risk premenopausal
- No proven chemopreventive agents for estrogen receptor-negative breast cancer
- Development of surrogate endpoint biomarkers which correlate with breast cancer risk and response to therapy

S0812: Vitamin D supplementation in high-risk premenopausal women

Eligibility:

- **5-yr Gail risk ≥1.67% or lifetime risk ≥20% (Gail, Claus, BRCAPro, IBIS)**
- **ADH, ALH, LCIS, DCIS**
- ***BRCA1/2, PTEN, p53* mutation**
- **stage I-II breast CA, >5yrs in remission**
- **MD >50%**

Premenopausal, Age 18-50
Baseline MD >10%
Serum 25(OH)D ≤32ng/ml
(N = 208)

RANDOMIZE

→ **Cholecalciferol (D3) 20,000 IU weekly x 1yr**

→ **Vitamin D3 600 IU qd**

→ **Matching placebo x 1yr**

Baseline data collection:
Mammogram
Core breast biopsy
Blood

Follow-up data collection:
Mammogram
Core breast biopsy
Blood

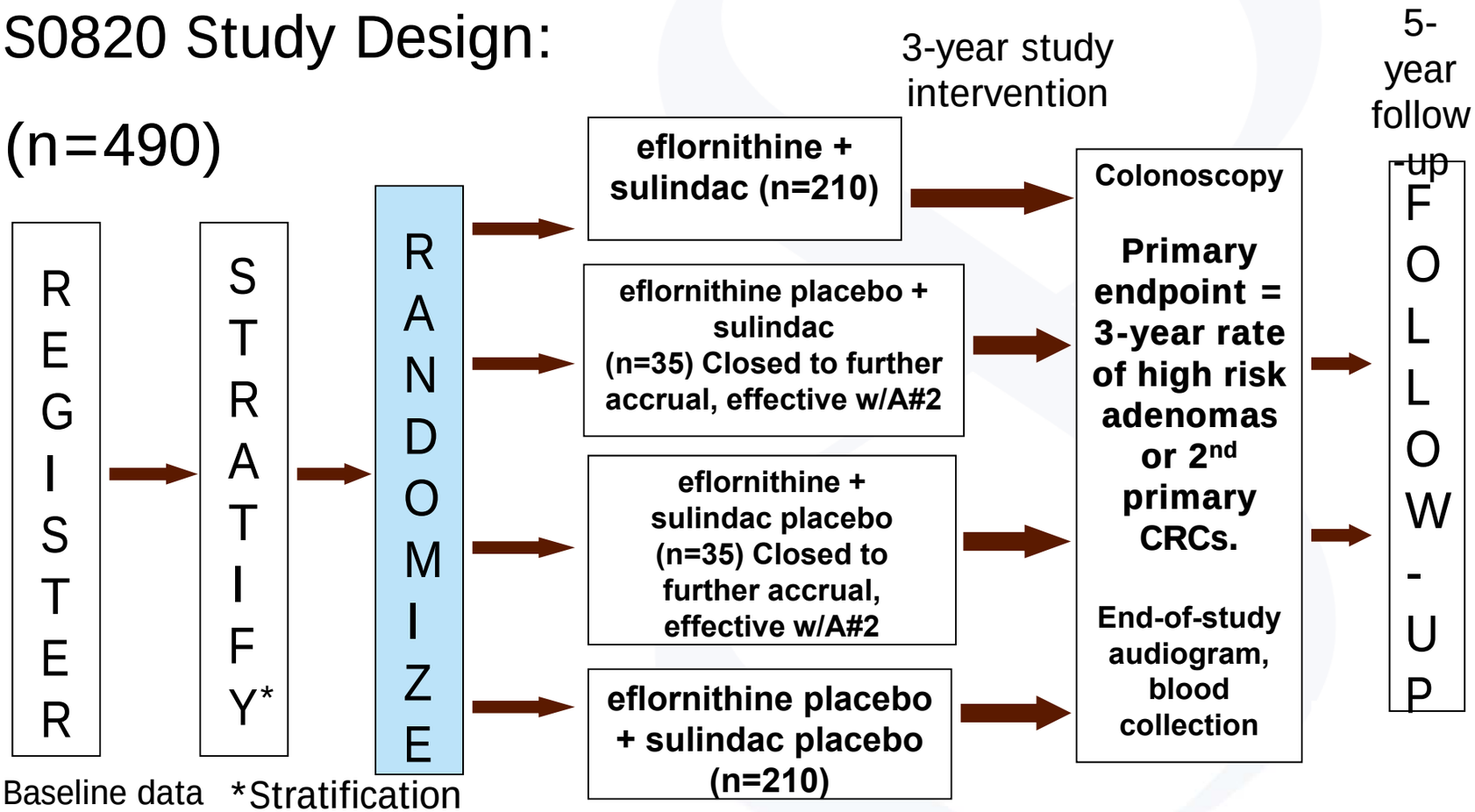
Primary Endpoint: Change in mammographic density at 1yr
Secondary Endpoints: Serum and tissue-based biomarkers, toxicity

Rationale for S0820

- Adenomatous polyps are a useful surrogate endpoint for colorectal cancer incidence.
- Low-dose combination chemoprevention regimens may increase efficacy with less toxicity.
- Cancer survivors are an important target population for secondary prevention trials.

S0820 Study Design:

(n=490)



Baseline data collection, audiogram, blood, CT-scans, & colonoscopy at Year-1 post resection

*Stratification by stage

PI: Zell

Activated: 3/1/13

Registrations: 162

Pre-registered: 407

Accrual Rate: 5/mo

Accrual Goal: 8/mo

Est. End Accrual: 3/21

SWOG Leading cancer research. **Together.**

Prevention and Epidemiology

- **Implementation Science**
  - S1711: Decision support to increase chemoprevention among women with atypical hyperplasia and lobular carcinoma *in situ*
- **Secondary Prevention**
  - Arun: Mammographic density changes with pembrolizumab in S1418
  - Brenner: Randomized biomarker study of aspirin and aromatase inhibitors in obese women with breast cancer
- **Young Investigators**
  - Connolly: IORT vs. WBXRT for DCIS
  - Nappi: miR-371 for tumor surveillance in testicular cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goserelin for Ovarian Protection during Breast-Cancer Adjuvant Chemotherapy

Halle C.F. Moore, M.D., Joseph M. Unger, Ph.D., Kelly-Anne Phillips, M.D., Frances Boyle, M.B., B.S., Ph.D., Erika Hitre, M.D., David Porter, M.D., Prudence A. Francis, M.D., Lori J. Goldstein, M.D., Henry L. Gomez, M.D., Carlos S. Vallejos, M.D., Ann H. Partridge, M.D., M.P.H., Shaker R. Dakhil, M.D., Agustin A. Garcia, M.D., Julie Gralow, M.D., Janine M. Lombard, M.D., John F. Forbes, M.B., B.S., Silvana Martino, D.O., William E. Barlow, Ph.D., Carol J. Fabian, M.D., Lori Minasian, M.D., Frank L. Meyskens, Jr., M.D., Richard D. Gelber, Ph.D., Gabriel N. Hortobagyi, M.D., and Kathy S. Albain, M.D., for the POEMS/S0230 Investigators

N ENGL J MED 372;10 NEJM.ORG MARCH 5, 2015

S0230: Prevention Of Early Menopause Study (POEMS)

- **Study population:** Premenopausal women, age 18-49, operable stage I-IIIA ER-/PR- breast cancer, treatment with cyclophosphamide-containing regimen *(N=257)*
- **Study intervention:** Chemotherapy with GnRH agonist, goserelin 3.6mg SQ q4wk, vs. chemotherapy alone
- **Primary endpoint:** Ovarian failure rate at 2yrs, amenorrhea for at least 6mo and serum FSH

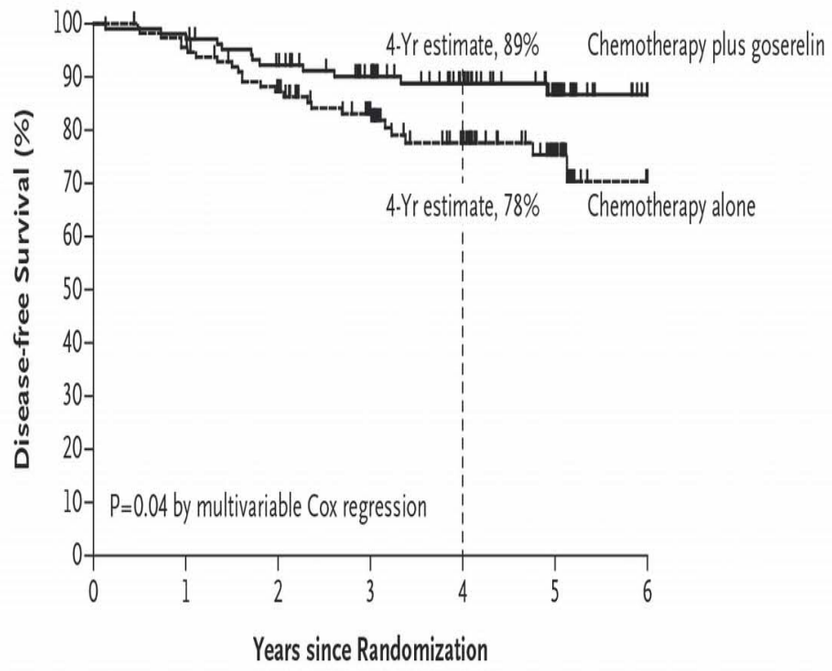
S0230: Results

- **Ovarian failure rate:** 8% for chemotherapy + goserelin group vs. 22% for chemotherapy alone (OR=0.30; 95% CI=0.10-0.87)

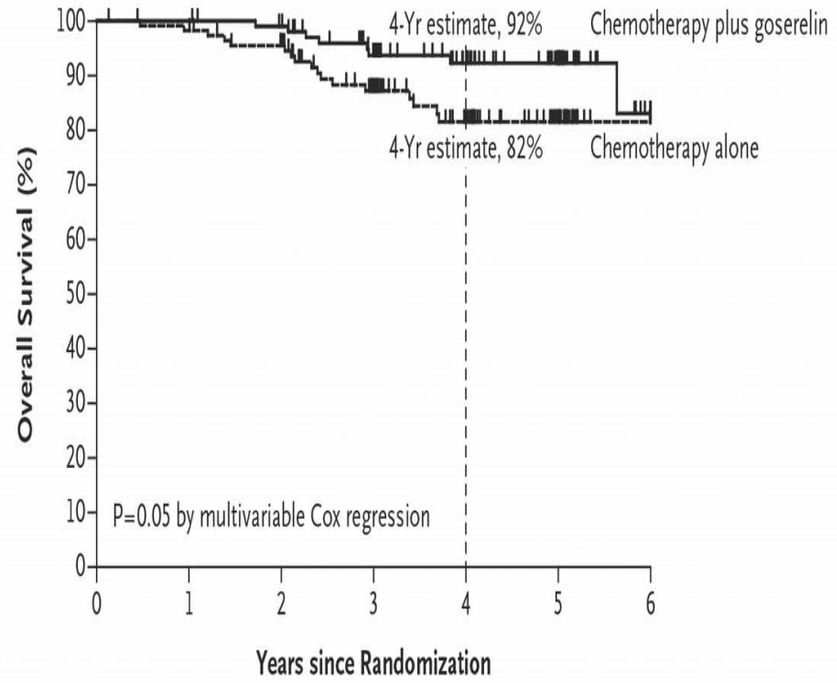
Table 3. Pregnancy Outcomes.

Outcome	Chemotherapy Alone (N=113)	Chemotherapy plus Goserelin (N=105)	Odds Ratio with Goserelin	P Value*
Attempted pregnancy — no. of patients (%)	18 (16)	25 (24)	1.78	0.12
Achieved pregnancy — no. of patients (%)	12 (11)	22 (21)	2.45	0.03
≥1 delivery — no. of patients (%)	8 (7)	16 (15)	2.51	0.05
Delivery or ongoing pregnancy — no. of patients (%)	10 (9)	19 (18)	2.45	0.04
Babies born — no.†	12	18		
Ongoing pregnancies at last report — no.	3	5		
Adverse pregnancy event — no. of events				
Miscarriage	5	4		
Elective termination	3	2		
Delivery complication	2	2		

S0230: Results



No. at Risk							
Chemotherapy plus goserelin	105	103	94	80	59	37	5
Chemotherapy alone	113	109	94	72	49	26	5



No. at Risk							
Chemotherapy plus goserelin	105	105	101	83	61	37	6
Chemotherapy alone	113	111	102	77	53	28	6

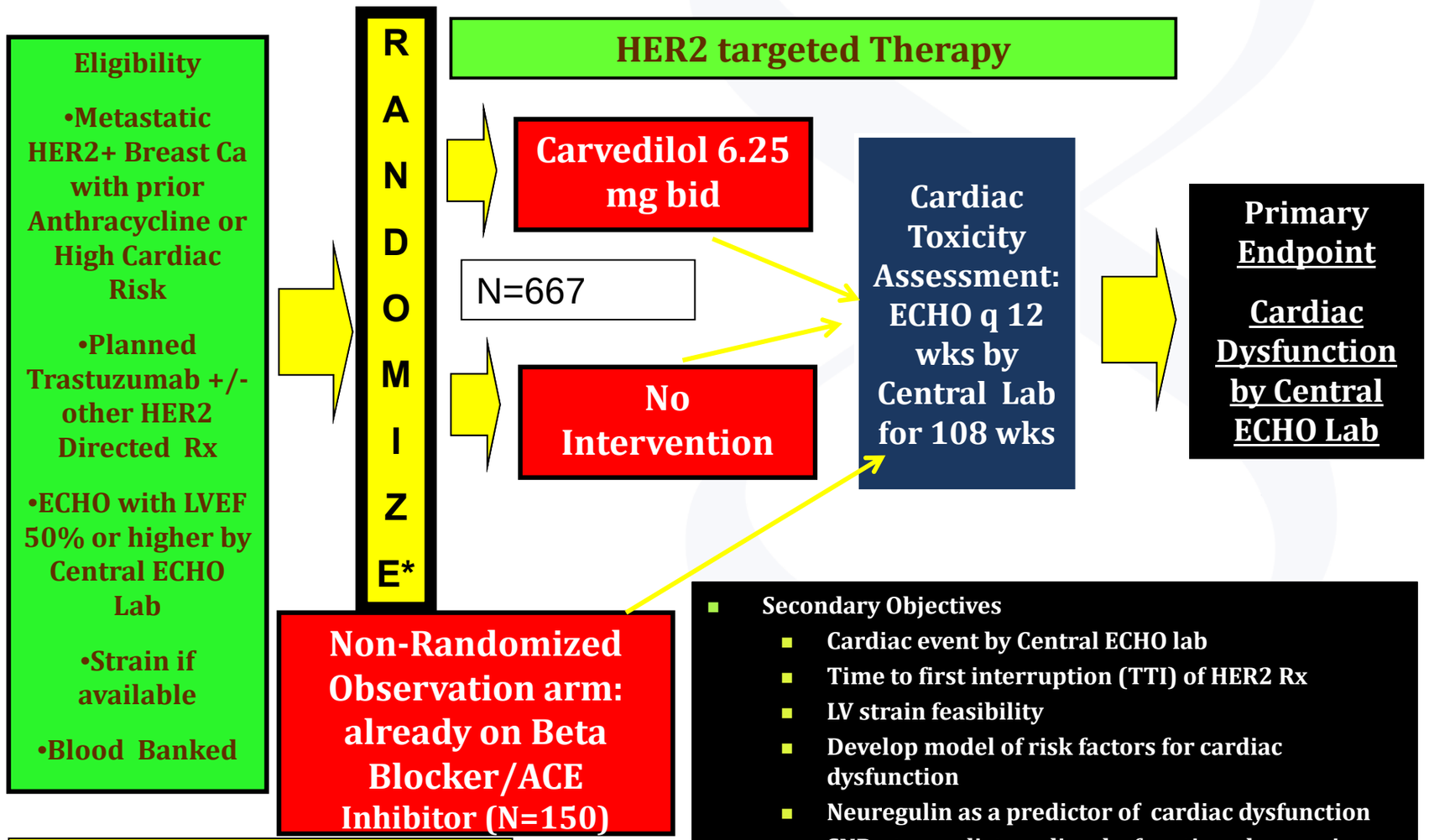
S0230: Conclusions

- Co-administration of a GnRH agonist with chemotherapy is an important option for fertility preservation in female cancer patients.
- Improved rates of DFS and OS with goserelin was unexpected in women with ER-negative breast cancer.
- Ongoing POSITIVE (Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer) study

Cancer Therapy-Related Cardiotoxicity

- With improvements in cancer treatments and increased survival, late affects and competing comorbidities are important survivorship concerns.
- Cancer treatments with adverse cardiovascular effects: anthracyclines, chest irradiation, HER2-targeted therapies, TKIs, anti-angiogenic agents, aromatase inhibitors
- Many cancers have shared risk factors with cardiovascular disease.

Schema for S1501



PIs: Floyd, Leja

Cancer Survivorship

- **Sexual/Gender-Based Health**
  - Dizon: Flibanserin to improve desire in women with cancer
  - Dorff: Testosterone replacement for hypogonadal symptoms in prostate cancer survivors
- **Cardiovascular Health**
  - S1008: Weight loss intervention in breast and colorectal cancer survivors
  - S1713: Text intervention to improve cardiovascular health in breast cancer survivors
  - Reding (YITC): Blood pressure monitoring with TKI use in RCC
- **Palliative Care**
  - S1316: Management of malignant bowel obstruction
  - Sun: Palliative care planning intervention for pancreatic cancer

Summary

- Cancer prevention is an important strategy to decrease cancer burden in LMICs.
- More efficient early phase chemoprevention trials with surrogate endpoints may facilitate drug development for cancer prevention.
- Need to address late effects and quality of life among cancer survivors.
- Opportunities for cancer prevention and survivorship ancillary studies within SWOG therapeutic trials.

SWOG

NCI National Clinical Trials Network

NCI Community Oncology Research Program