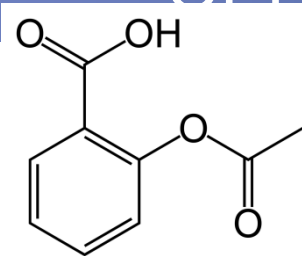


Proposal for Review

STICs and STONES: Prospective Assessment of Aspirin in Chemoprevention of high risk Ovarian Cancer (CCTG OV.24)

A RANDOMIZED TRANSLATIONAL WINDOW OF OPPORTUNITY TRIAL

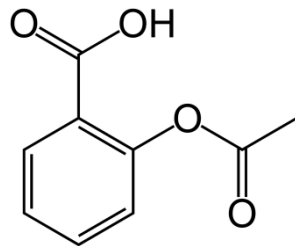


Stephanie Lheureux, Katherine Karakasis, Patricia Shaw, Harriet Richardson, Elisabeth Eisenhauer, Hal Hirte, Daliah Tsoref, Barry Rosen and Amit Oza

Study proposal

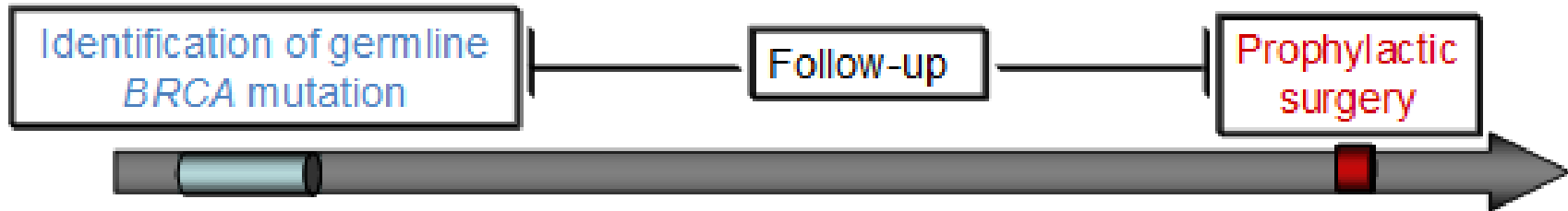
A phase II, double blind, placebo- controlled, randomized trial to compare regular use of low-dose aspirin versus placebo in women with germline BRCA1/2 mutations.

In both arms, prophylactic surgery will be performed in the expected timing as part as the standard of care.

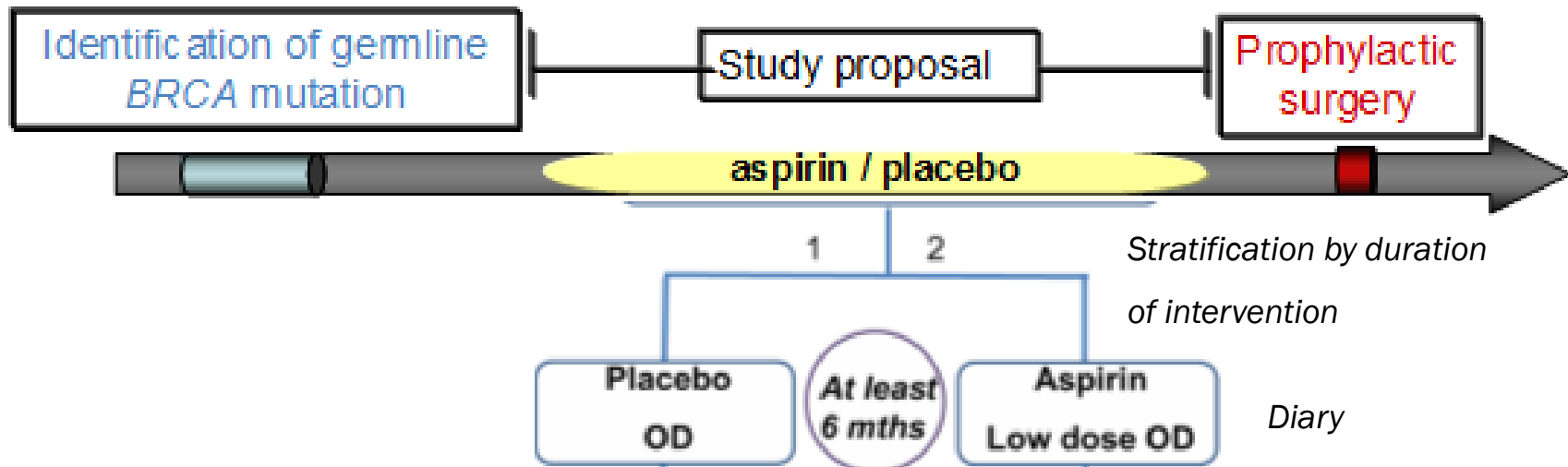


Hypothesis: Regular use of low-dose aspirin in women with inherited BRCA1/2 mutations will decrease the occurrence of ovarian cancer precursor lesions observed in the fallopian tube at the time of the prophylactic surgery.

Standard of Care



Study Proposal



■ Primary

Presence/absence and numbers of cancer precursor lesions identified by Central Pathology review in the fallopian tube in resected specimens of patients who receive a minimum of 6 months of either low dose aspirin or placebo:

- Occult (early) carcinoma
- Serous tubal intraepithelial carcinoma (STIC)

■ Secondary

- To identify the non-invasive tubal lesions: the p53 signature
- To elucidate the linkage between tumorigenesis and microenvironment
 - Hormone stimulation
 - Inflammatory mediators involved in ovulation
 - COX1/2 - VEGF
- To assess the credibility/ acceptance of the drug intervention and monitor serum ASA levels

■ Hypothesis

➤ Control: 15% occurrence of pre-& early-malignant lesions

- 6% occult carcinoma
- 7-10% STICs

Geoge SH, Front Oncol 2014

➤ Aspirin: 40% risk reduction

Trabert D, J Natl Cancer Inst 2014

■ Sample Size

Placebo Group Pre-lesion rate (%)	Aspirin Group Pre-lesion rate (%)	Absolute difference	Type I error rate	N1:N2 (Total)
15	9	6.0	0.20	248:124 (372)

2:1 allocation; Type I error 1-sided; 40% relative risk reduction

Drop off 10%: 414 patients for inclusion

Feasibility: Estimated Accrual 200/year

Province	Centre	PI	# pt with prophylactic salpingo oophorectomy	Eligible subjects annually
ALTA	Cross Cancer Inst	V Capstick	20	6
BC	BCCA Vancouver	D Miller	25	20
MB	Cancer Care Manitoba: Winnipeg	L Lotocki	10	5
NFLD	D.H. Bliss Murphy Cancer Centre	P Power	15	10
ON	Ottawa Hospital	M Fung Kee Fung		
ON	Jurvinski Cancer Centre			
ON	PMH	B Rosen	40	40
ON	London Health Sciences Centre	J McGee	20	10
QC	CHUM	Sauthier	12	8
QC	CHUQ	M Plante	20	most
SASK	Saskatoon	C Giede	10	70%

Intergroups: ANZGOG, GINECO, MRC
 ?? NRG, NSGO

Current Status of Trial

- Protocol written
- Database specifications finalized
- Drug Supply: Discussions ongoing with regulatory authority and drug manufacturer: stability testing and study supply capsule composition
- Planned trial activation in Canada: first quarter 2017
- Collaborating Groups must self fund for participation