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Consortia Partnerships:
The Benefits of Consortia Working Together

Carey K. Anders, MD

November 30, 2012

Outline

- Definition of Consortia
- Successful Examples
  - NC Myeloma Study Group
  - Geriatric Oncology Consortia
  - Translational Breast Cancer Research Consortia
- Real-world application
  - LCCC 0919/TBCRC 018

Definition of Consortia

- A **consortium** is an association of two or more individuals, companies, organizations or governments (or any combination of these entities) with the objective of participating in a common activity or pooling their resources for achieving a common goal.

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Per Wikipedia.com

Cancer & Aging Research Group (CARG)

The mission of the Cancer and Aging Research Group is to join geriatric oncology researchers across the nation in a collaborative effort of designing and implementing clinical trials to improve the care of older adults with cancer.

Webpage: www.mycarg.org/home

Meet the CARG Researchers

Arti Hurria, M.D.

Roles: CARG Study 1,
National PI & U13 Grant, PI
Specialty: Geriatric Oncology; Breast Cancer
Institution: City of Hope Comprehensive Cancer Center

Hyman B. Muss, M.D.

Specialty: Breast Cancer and Geriatric Oncology
Institution: University of North Carolina, Chapel Hill

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**Two among n = 18 investigators across 14 different sites both in and outside the US

Ongoing CARG Studies

1. Determining the Utility of an Assessment Tool for Older Adults with Cancer Protocol Summary on ClinicalTrials.gov Details (Login Required)

2. Clinical and Biological Predictors of Chemotherapy Toxicity in Older Adults Protocol Summary on ClinicalTrials.gov Details (Login Required)

3. Tolerability of the Combination of Lapatinib and Trastuzumab in Adults Aged 60 or older with HER2 Positive Metastatic Breast Cancer Protocol Summary on ClinicalTrials.gov Details (Login Required)

4. Longitudinal Impact of Adjuvant Chemotherapy on Functional Status, Comorbidity and Quality of Life Protocol Summary on ClinicalTrials.gov Details (Login Required)

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Additional Resources per CARG

- Links to over 10 completed studies/publications
- Grant opportunities
- Educational Resources
- Chemotherapy Toxicity Calculator
- Annual meeting information
- Mentoring skills….and more!

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North Carolina Myeloma Study Group

- Goal: Conduct cutting-edge clinical trials for patients with advanced multiple myeloma

Pete Voorhees, MD
UNC Chapel Hill

Cristina Gasperetto, MD
Duke University

David Hurd, MD
Wake Forest University

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LCCC 0715

Title: Phase I study of Doxil, Bortezomib and Vorinostat to treat patients with relapsed/refractory multiple myeloma (PI: Voorhees)

Cohorts 1-3

Days	1	2-3	4	5-7	8	9-10	11	12-21	
Vorinostat			X →						
Bortezomib	X		X		X		X		
PLD			X						

21-day cycle
Bortezomib 1.3 mg/m^2 IV on days 1, 4, 8 and 11
PLD 30 mg/m^2 IV on day 4

Dose Level for Vorinostat	Mg PO daily
Dose -1	200mg/Doxil 22.5mg/m2
Dose 1	200mg
Dose 2	300mg*
Dose 3	400mg*

*Cohorts 4 – 5, examine DURATION of Vorinostat, days 1 - 14

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Cohort 3A

Days	1	2	3	4	5	6	7	8	9	10	11	12	13-21
Vorinostat	X	X		X	X			X	X		X	X	
Bortezomib	X			X				X			X		
PLD				X									

21 -day cycle
Bortezomib 1.3 mg/m^2 IV on days 1, 4, 8 and 11
PLD 30 mg/m^2 IV on day 4

Due to promising results at dose level 4 (PR 72%), yet unacceptable thrombocytopenia, Cohort 3A designed
Dose of Vorinostat = 400mg orally on Days as per above

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LCCC 0715: Results

MTD: Vorinostat in combination with PLD and bortezomib was 400 mg given on days 4 – 11

Response: 65% among n = 31 evaluable patients; 45% in bortezomib-refractory disease

LCCC 0715 supports *feasibility* of successful execution of complex phase I clinical trials across well-coordinated Consortium!

Phase I VB/PLD in Relapsed/Refractory MM [22]			
AE*	All AEs (%)	Grade 3 (%)	Grade 4 (%)
Neutropenia	59	34	3
Anemia	34	0	0
Thrombocytopenia	94	16	31
Fatigue	63	16	0
Anorexia	47	3	0
Nausea	78	9	0
Vomiting	50	9	0
Diarrhea	81	16	3
Constipation	50	0	0
Peripheral neuropathy	38	6	0
Hand Foot Syndrome	25	9	0
*AEs ≥ possibly related to protocol therapy			

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Voorhees, P.M., et al., ASH Annual Meeting Abstracts, 2010. **116**(21): p. 1955.

Translational Breast Cancer Research Consortium
An Academic/Foundation Partnership

Antonio C. Wolff, MD
Professor of Oncology
The Johns Hopkins Kimmel Cancer Center
awolff@jhmi.edu

Background of TBCRC

- Breast cancer as an umbrella of phenotypes
  - Diverse natural history and diverse targets
- Trials that are biology-driven
  - Procurement of well-annotated biospecimens
  - Access to novel imaging and biological assays
- Too small and too intensive for cooperative groups, too large for any single institution
- Long-standing informal collaborations among breast cancer SPOREs to conduct clinical trials
  - Eg, Avon/NCI Partners in Progress Program
- Need for a nimbler, independent, and ready-on research enterprise

Mission Statement

"The TBCRC is a cooperative effort of clinical trialists, translational scientists, and patient advocates from academic medical centers dedicated to innovative, high impact and biologically-driven clinical research. The overarching mission of the Consortium is to lessen the burden of breast cancer by using a collaborative and multidisciplinary approach to improve the understanding of breast cancer biology and test new therapeutic strategies. The Consortium will conduct clinical trials in the preoperative, pre-surgical, metastatic, and preventive settings. Consortium members work together closely to speed completion of clinical trials, share biologic specimens and clinical data, and identify new areas for research."

TBCRC Member Institutions

Baylor College of Medicine
Dana-Farber/Harvard CC
Duke University
Georgetown University
Indiana University
Johns Hopkins Kimmel CC
Mayo Clinic
MD Anderson Cancer Center
Memorial Sloan Kettering CC
University of Alabama, Birmingham
University of California, San Francisco
University of Chicago (2007)
University of Michigan (2009)
University of North Carolina, Chapel Hill
University of Pittsburgh (2009)
Vanderbilt University

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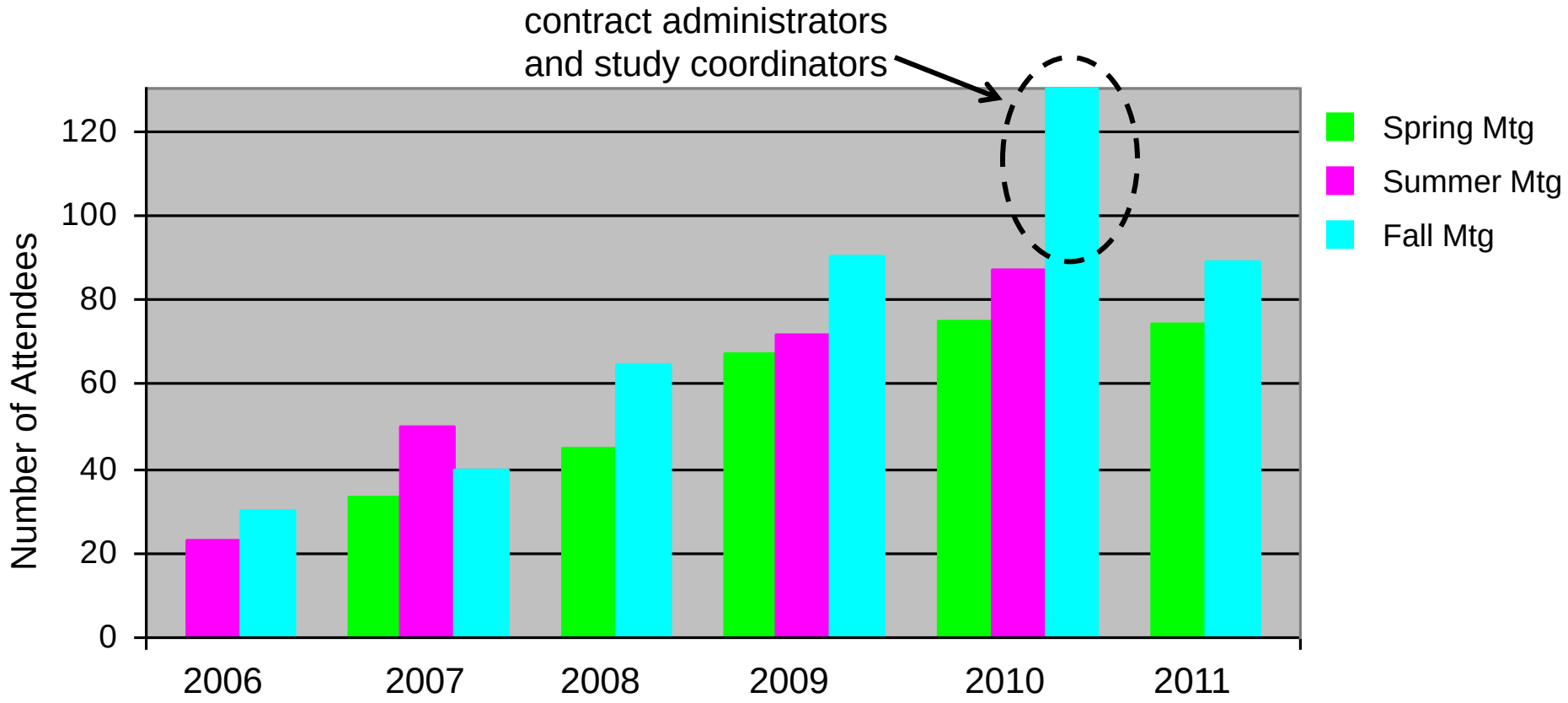
TBCRC Member Involvement



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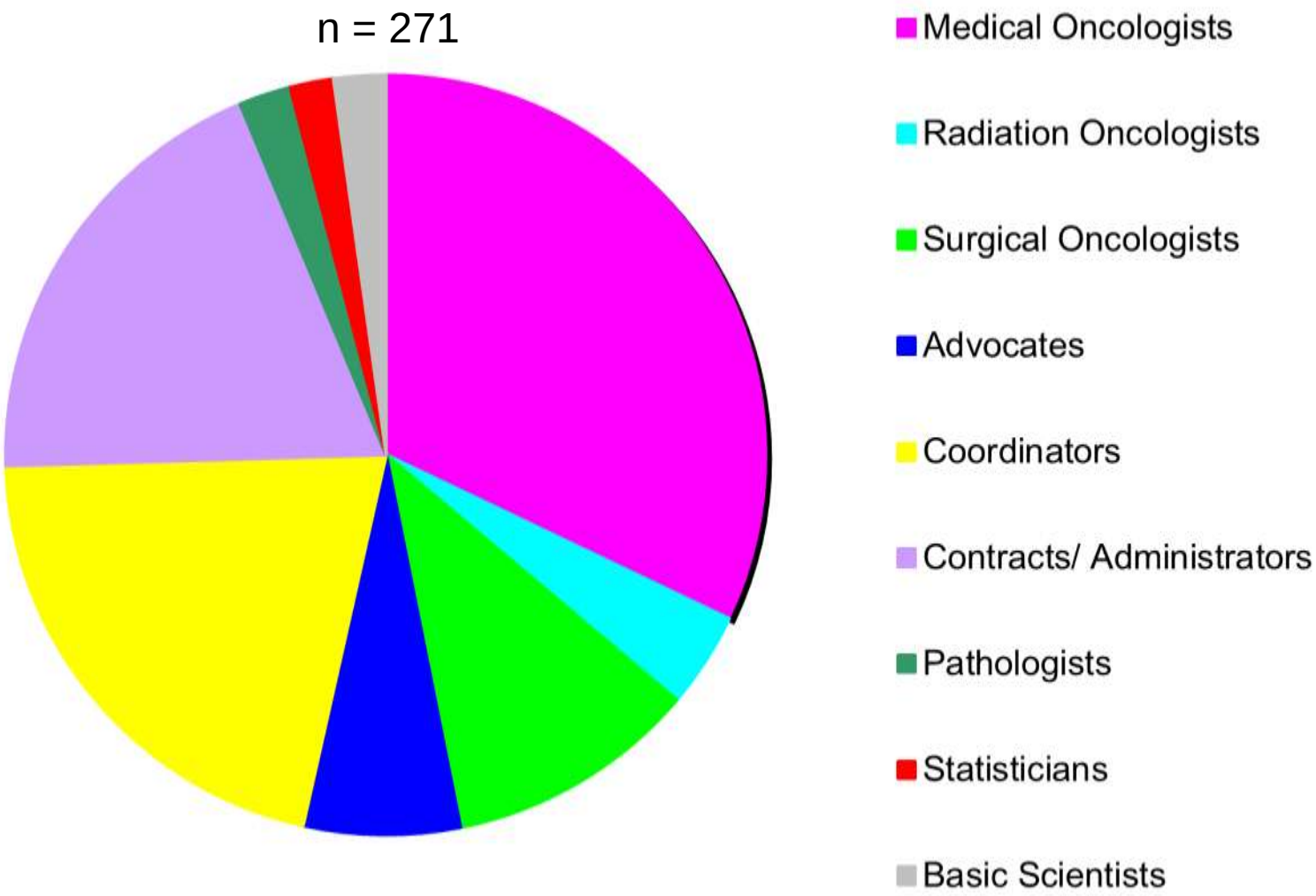
The Proverbial TBCRC Village …



TBCRC Working Groups

- First established in October 2007
- Goal: where the "lion-share" of the concept development takes place, open membership, common interests
- 4 disease-based WGs
  - Endocrine Resistance WG
  - HER2 Resistance WG
  - Locoregional Disease WG
  - Triple Negative WG
- Correlative Science WG
- 4 supporting WGs
  - Patient Advocate WG
  - Study Coordinator WG
  - Statistical Advisory Group (established 2009)
  - Contracts & Administrators WG (established 2010)

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TBCRC Organizational Structure

Steering Committee

Arteaga, Carey, Davidson, Hilsenbeck, Hortobagyi, Hudis, Ingle, Norton, Winer, Wolff

Working Groups

"where the action is …"

Protocol Review Committee

16 PIs, 1 advocate, 1 statistician

Protocol Evaluators

2 scientists, 1 statistician, 1 advocate, 1 study coordinator

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Accrual - Active & Completed/Closed Trials

	Brief Titles	Accruals (as of 2/3/12)	Targeted Accrual
TBCRC 001	TN: Cetuximab ± Carboplatin	113	100
TBCRC 002	Letrozole ± Bevacizumab	38	75
TBCRC 003	Lapatinib/Trastuzumab	89	116
TBCRC 004	Letrozole/Lapatinib	6	36
TBCRC 005	DNA Methylation as a Biomarker	182	180
TBCRC 006	Lapatinib/Trastuzumab +/- Endocrine Therapy	66	66
TBCRC 007	MPA +/- Cy MTX	31	30-50
TBCRC 008	Carbo nab-Paclitaxel +/- Vorinostat	68	68
TBCRC 009	TN: Carboplatin or Cisplatin	83	82
TBCRC 010	Dasatinib and ZA for Bone Mets	23	28
TBCRC 011	AR+, ER/PR-: Bicalutamide	27	28
TBCRC 012	ABCDE	25	660

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CONTINUED TO NEXT SLIDE……

Accrual - Active & Completed/Closed Trials

	Brief Titles	Accruals (as of 2/3/12)	Targeted Accrual
TBCRC 013	Stage IV Registry	113	140
TBCRC 014	Retrospective Adjuvant Signature	137 (retrospective)	250
TBCRC 015	Capecitabine Toxicity Predictor	154	250
TBCRC 016b	Phase III Iniparib Companion	18	-
TBCRC 017	MRI Prediction of Preop Response	769 (retrospective)	750
TBCRC 018	BSI-201 + chemo in TN Brain Mets	33	40
TBCRC 019	Tigatuzumab and nab-Paclitaxel	60	60
TBCRC 020	Lobular Neoplasia	33	78
TBCRC 021	BMS-754807 ± Letrozole	27	80
TBCRC 022	Neratinib	0	45
TBCRC 023	Lapatinib/Trastuzumab ± Endocrine Therapy for 12 v 24 weeks	10	82
TBCRC 024	Veliparib & radiation	0	30
	TOTALS	2105	3274-3294

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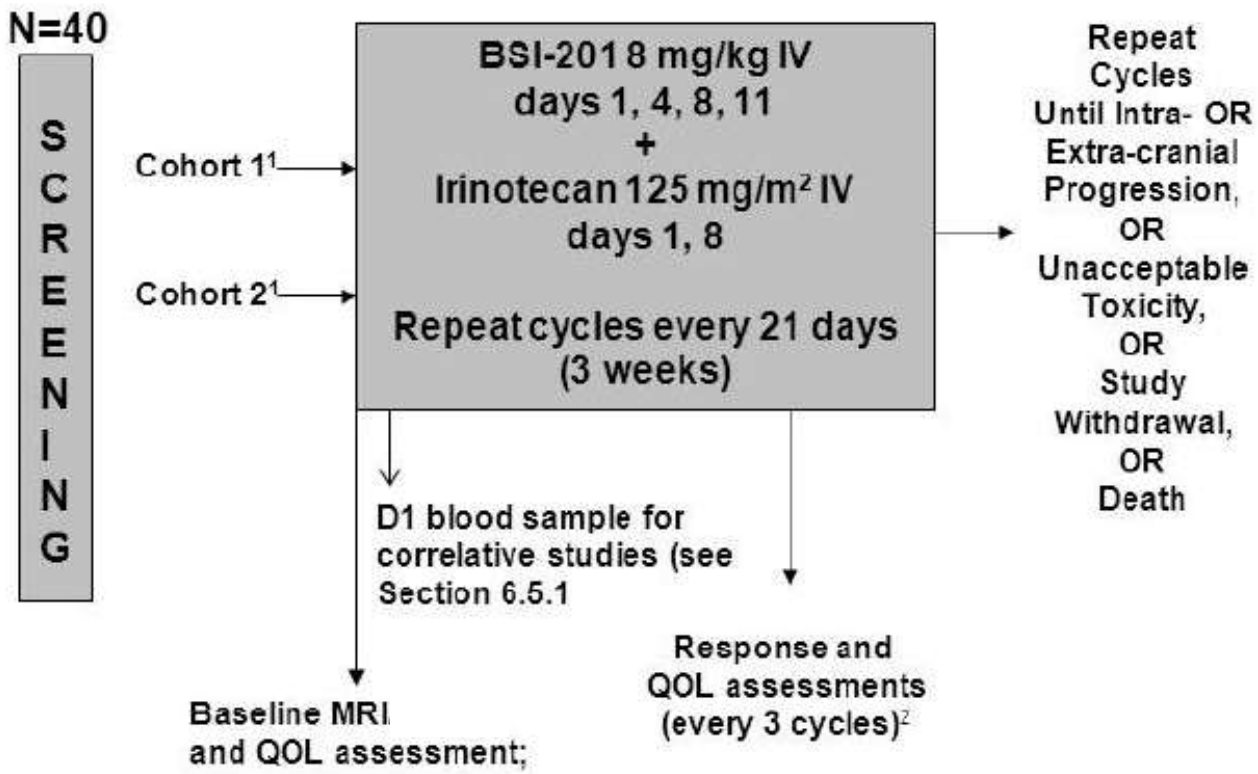
Study Schema for TBCRC 018/LCCC0919

"Phase II study of irinotecan/iniparib to treat patients with progressive TNBC brain metastases"



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[1]Cohort 1 = prior cranial radiation
Cohort 2 = cranial radiation naïve

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Histologically-confirmed triple negative adenocarcinoma of the breast with brain lesion (> 5mm) on radiographic imaging.

2. Cohort 1: Patients with unequivocal evidence of new and/or progressive brain metastases AFTER prior intracranial radiation therapy

-OR -

Cohort 2: Intracranial radiation-naïve patients for whom ICR is not emergently indicated (at treating physician's discretion and in collaboration with local therapist)

3. No limit to prior therapies with last anti-cancer treatment ≥ 2 weeks from protocol-based therapy provided all toxicities have resolved to ≤ Gd1.

4. Stable dose of steroids for ≥ 7 days.

Exclusion Criteria:

1. Prior allergic reaction to BSI-201 or irinotecan. Prior irinotecan and BSI-201 allowed.

2. Evidence of hemorrhage or impending herniation on baseline brain imaging.

3. Evidence of diffuse leptomeningeal disease on brain MRI or by previously documented CSF cytology

4. Contraindication to gadolinium-enhanced MRI imaging.

5. Pregnant, breast-feeding, PS > 2or clinically-significant organ dysfunction

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Study Objectives

Primary Objective:

To evaluate the efficacy Inparib (BSI-201, BiPar/Sanofi) in combination with irinotecan to treat brain metastasis arising from TNBC as measured by intracranial TTP (by modified RECIST) or extracranial TTP (by RECIST 1.1)*

*whichever occurs first

Secondary Objectives

a) To evaluate the safety and tolerability of BSI-201 in combination with chemotherapy

b) To evaluate intracranial objective response rate (ORR) determined by modified RECIST criteria, volumetric analysis, and central nervous system (CNS) Composite Response Criteria

c) Evaluate extracranial response rate by RECIST 1.1 criteria

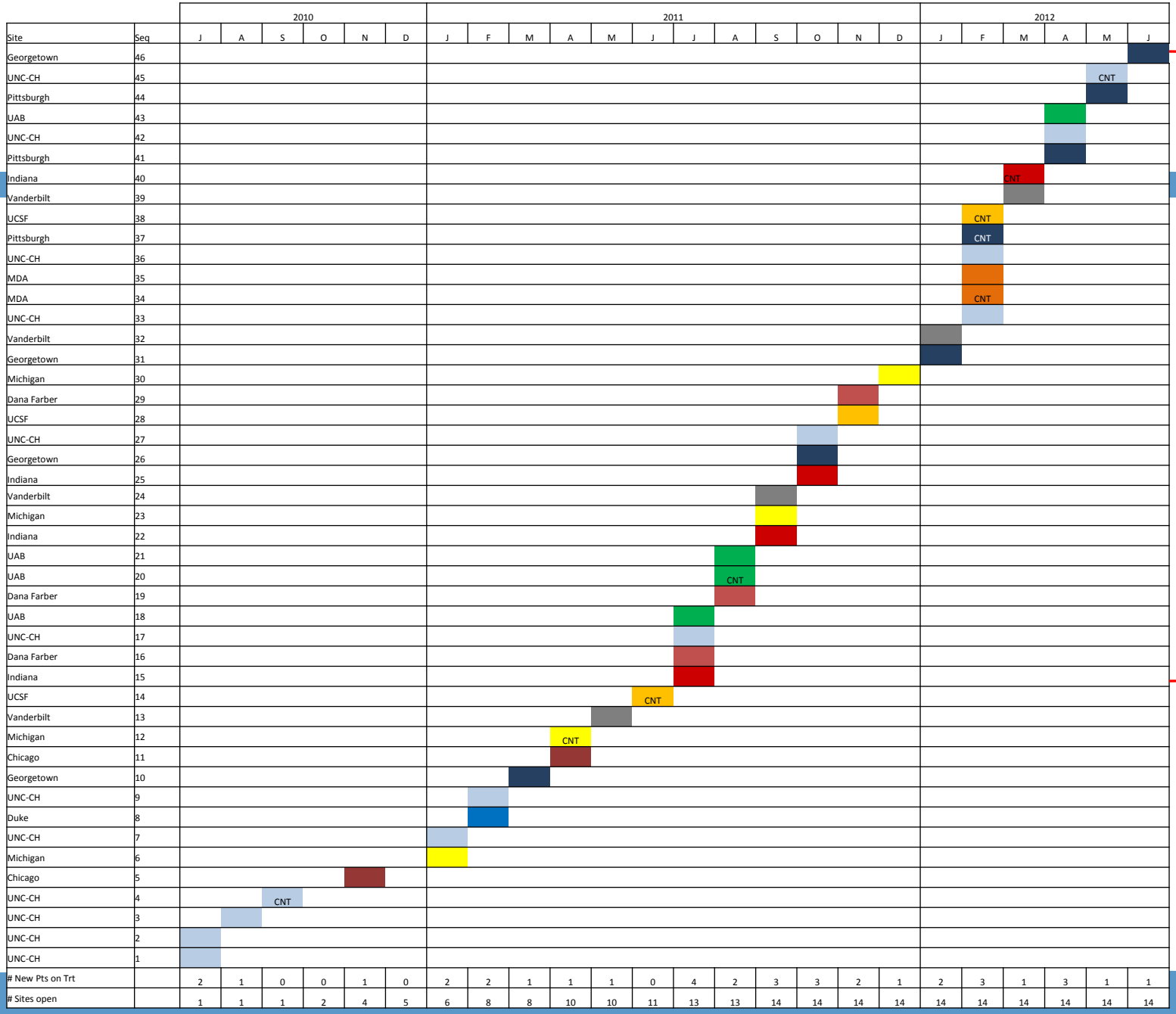
d) Evaluate progression free survival (PFS) and overall survival (OS)

e) Evaluate the impact of BSI-201 on quality of life the FACT-B and FACT Br questionnaires

TBCRC "in action….LCCC0919/TBCRC 018"

- *Spring 2009*: Concept to discussed on TBCRC TNBC WG calls
  - *Interest expressed; decision made to bring to in-person meeting*
- *Fall 2009*: Concept to in person TBCRC meeting
  - *Discussed alternate chemotherapy backbone; drafted protocol*
- *July 2010*: First patient on study
- *August 2012*: Last patient on study
- *February 2013*: Anticipate ASCO abstract submission; manuscript to follow

Final Accrual TBCRC 018/LCCC 0919 (July 2010 – August 2012)



Average 3 – 4 pts/ month once all sites activated

Total n = 46

CNT = 9

Eval. Pt = 33

Our Definition of Consortia

- A **consortium** is an association of two or more individuals, companies, organizations or governments (in our case medical centers/cancer centers) with the objective of participating in a common activity or pooling their resources for achieving a common goal (to improve patient's cancer-related outcomes).

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Per Wikipedia.com

Conclusions: Power of Consortia

- Aid in the conception, development and implementation of novel oncology studies
- Provide a mechanism for more efficient accrual to clinical trials
  - Particularly *niche* diseases such as BCBM
- Offers a forum for constructive feedback re: study design, etc.
- Unified goal to improve cancer-related outcomes

Thanks!

Questions?

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