ESMO Fellowship

Best Fellowship Project # 2

Hatem A. Azim Jr, MD, PhD

Institut Jules Bordet

Brussels, BE

Who Am I ?

- Egyptian
- Medical Oncologist – NCI Cairo
- Passion for research
- Seeking to build an international career in the field of cancer research

IEO
Istituto Europeo di Oncologia

During my training 2008

Introduction to the field **BC & pregnancy**

-Reviews

-Case reports

-Review papers

-Attend clinics and MDT

-Establish hospital based series

"BC during pregnancy" "Pregnancy after BC"

ULB Institut Jules Bordet Instituut
réseau iris structuur

ESMO Translational Fellowship 2010

- Understand impact of pregnancy on BC Biology/Outcome
  - Gene expression
  - Sequencing
  - Protein based

Project: Genomic Profiling of breast cancer during pregnancy

Home institute: National Cancer Institute, Cairo

Host institute: Institut Jules Bordet, Brussels

CHALLENGES

- A clinician going to the lab
- No previous experience in micro-array / sequencing
- Working in your 3rd language !!!
- Work on grants/funding under tight timelines

CHALLENGES

- Settling in a new country
- New culture
- Paper work +++++
- Different weather !!!
- Family relocation

Keep up with your peers !!

ULB Institut Jules Bordet réseau iris structuur Instituut

Sherene LOI
Assoc. Professor, University of Melbourne

Michail IGNATIADIS
Faculty Staff, Institut Jules Bordet

Philippe BEDARD
Faculty Staff, Princess Margaret

Carmen Criscitiello
Medical Oncologist, European Inst of Oncology

Otto METZGER
Faculty Staff, Dana Farber

Kamal SAINI
Associate Director, Breast International Group

Fellowship Plan

Develop the ESMO project as a part of a PhD at the Institut Jules Bordet (Université Libre de Bruxelles; ULB) titled

"BC in young women: impact of pregnancy on biology & outcome"

- **Biology of BC in young women (Translational – gene expression)**
- **Biology of BC during pregnancy (Translational – gene expression, sequencing, protein)**
- **Pregnancy after breast cancer diagnosis (Clinical)**

Clin Cancer Res 2012;18:1341-1351

Predictive Biomarkers and Personalized Medicine

Clinical Cancer Research

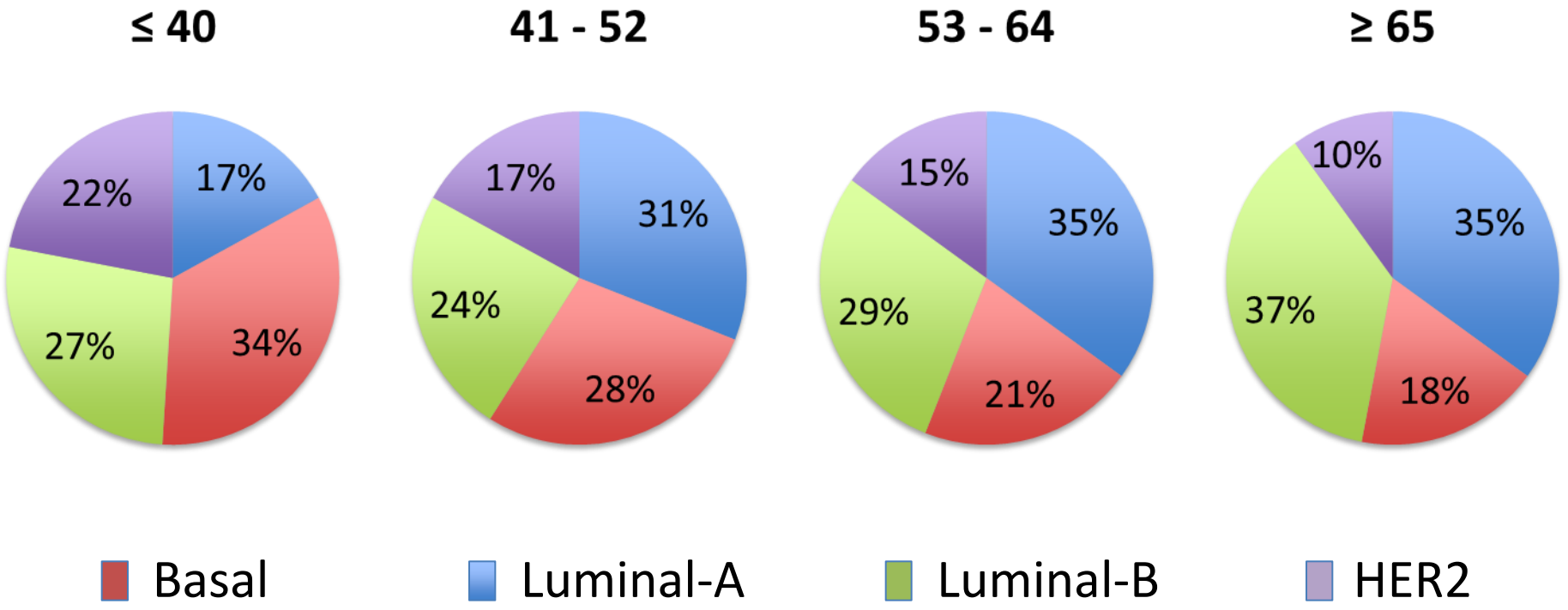
Elucidating Prognosis and Biology of Breast Cancer Arising in Young Women Using Gene Expression Profiling

Hatem A. Azim Jr[1], Stefan Michiels[1], Philippe L. Bedard[2], Sandeep K. Singhal[1], Carmen Criscitiello[1], Michail Ignatiadis[1], Benjamin Haibe-Kains[3], Martine J. Piccart[4], Christos Sotiriou[1], and Sherene Loi[1]

Oral Presentation

More ***Basal*** tumors and less luminal-A in young women

N=3,522



p<0.0001

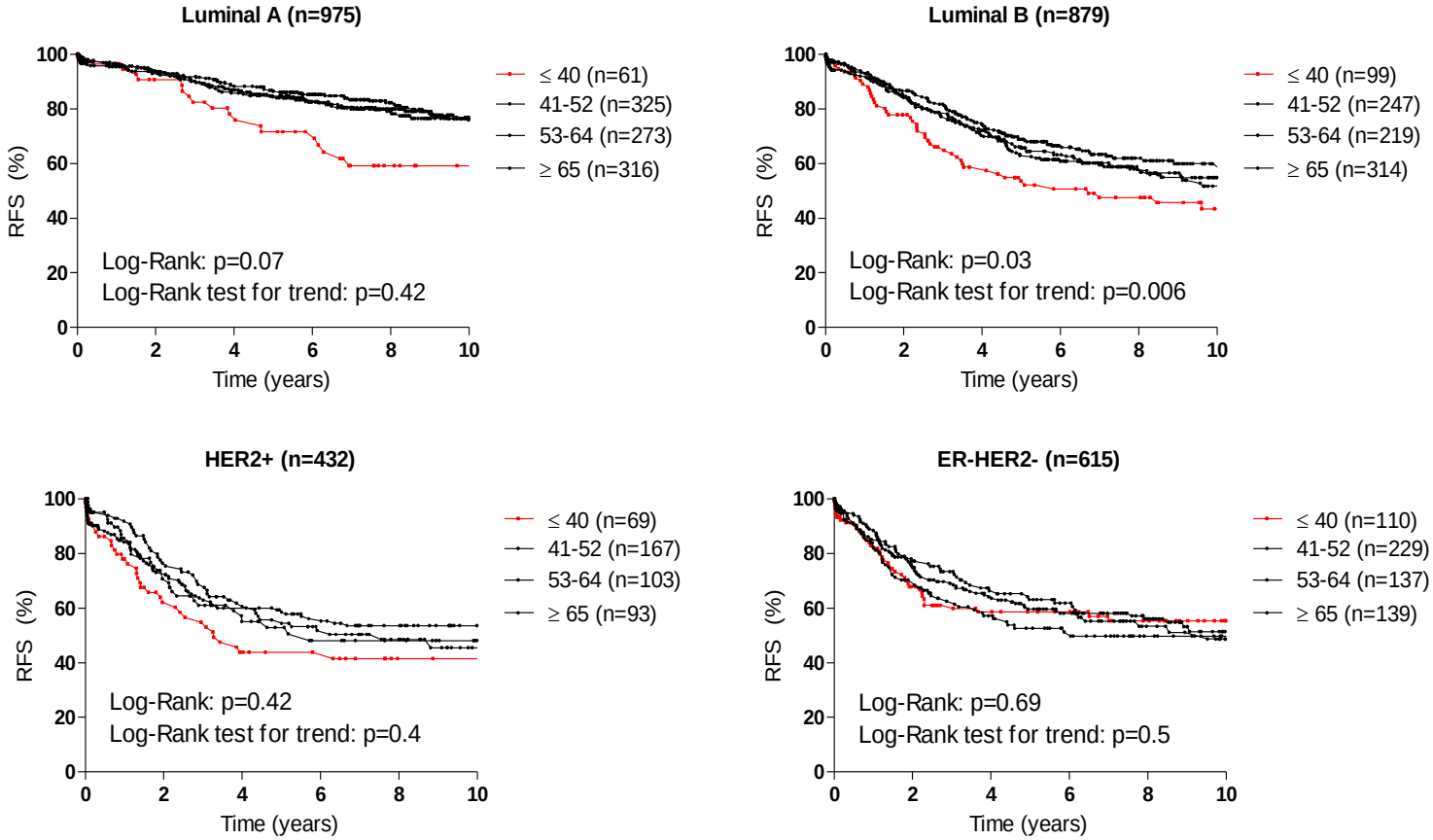
Azim HA Jr et al; CCR 2012

BC in the young is associated with poor prognosis ***independent*** of other possible confounding factors

	HR	95% CI	p-value
Age (≤ 40 vs. >40)	**1.3**	**1.1 – 1.6**	**0.004**
Tumor size (>2cm vs. < 2cm)	1.6	1.4 – 1.9	<0.001
Nodal status (N+ vs. N0)	1.7	1.5 – 2.1	<0.001
Histological grade (III vs. II vs. I)	1.5	1.3 – 1.7	<0.001
BC subtype (Basal vs. HER2+ vs. ER+/HER2-)	1.1	1.01 – 1.2	0.04
Treatment	1.3	1.1 – 1.5	0.04

Azim HA Jr et al; CCR 2012

A particular trend of poorer prognosis in ***luminal*** tumors



Azim HA Jr et al; CCR 2012

BC in young women is enriched with potential cancer targets

	Genes	Gene sets	Direction	Training set (n=1188)		Validation set (n=2334)	
				Effect of age adjusted to all covariates *	FDR	Effect of age adjusted to all covariates *	FDR
Apoptosis-related	**FAS** **CASP3** **BAD**		down	6.6E-03 2.2E-02 3.2E-02	0.03 0.08 0.11	3.9E-03 2.5E-02 1.7E-02	0.008 0.04 0.03
MAP kinase – related		**MAPK**	up	5.8E-07	<0.0001	5.9E-05	0.0002
mTOR/PI3K – related	**PDPk1**	**PIK3CA-GS**	up	2.1E-02 6.7E-09	0.08 <0.0001	7.6E-04 5.0E-11	0.002 <0.0001
BRCA-related	**BRCA1**	**BRCA1**	down up	3.8E-04 4.5E-03	0.003 0.02	4.4E-02 2.5E-03	0.06 0.006
Stem cell-related	**RANKL**	**MaSC**	up up	1.8E-10 1.5E-09	<0.0001 <0.0001	1.6E-06 3.2E-15	<0.0001 <0.0001
Luminal progenitor	**c-kit**	**Luminal progenitor**	up up	3.3E-13 1.1E-03	<0.0001 0.007	1.3E-07 1.9E-02	<0.0001 0.04

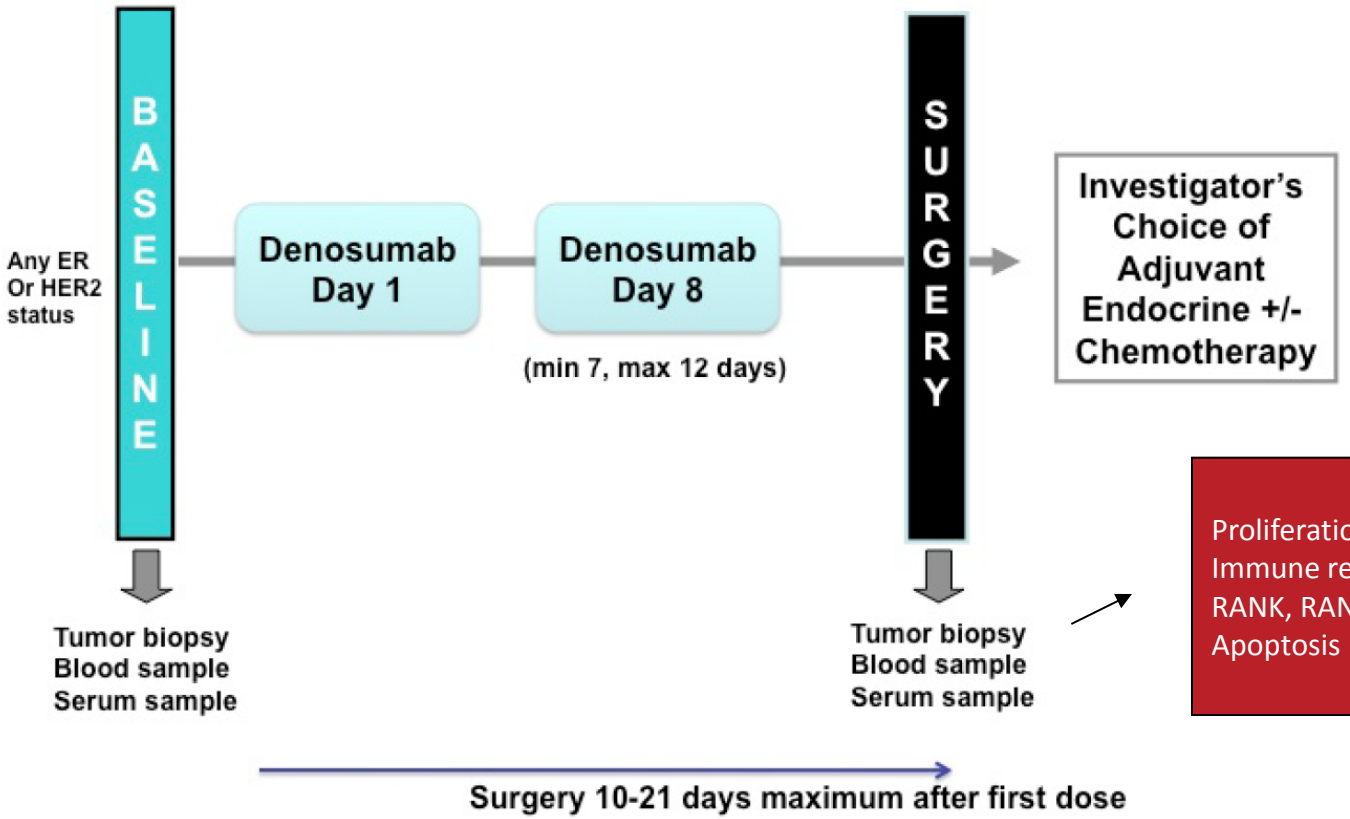
* Analysis adjusted for BC subtype, T, N, Grade

Azim HA Jr et al; CCR 2012

D-BEYOND

Denosumab Biological Effects in Young Women Diagnosed with Breast Cancer

Key eligibility
- Pre-menopausal
- Tumor size >1.5
- M0



26-30 September 2014, Madrid, Spain

esmo.org

Trial currently recruiting

Research grant from AMGEN

Clinical Trial Identifier: NCT01864798

MADRID 2014 ESMO congress

Research | H A Azim Jr et al. | Biology of breast cancer during pregnancy | Endocrine-Related Cancer (2014) 21, 545–554

Biology of breast cancer during pregnancy using genomic profiling

Hatem A Azim Jr[1,2], Sylvain Brohée[2], Fedro A Peccatori[3], Christine Desmedt[2], Sherene Loi[4,5], Diether Lambrechts[6,7], Patrizia Dell'Orto[8], Samira Majjaj[2], Vinu Jose[2], Nicole Rotmensz[9], Michail Ignatiadis[2,10], Giancarlo Pruneri[8], Martine Piccart[10], Giuseppe Viale[8] and Christos Sotiriou[2,10]

Oral Presentation

Funding

fnrs LA LIBERTÉ DE CHERCHER

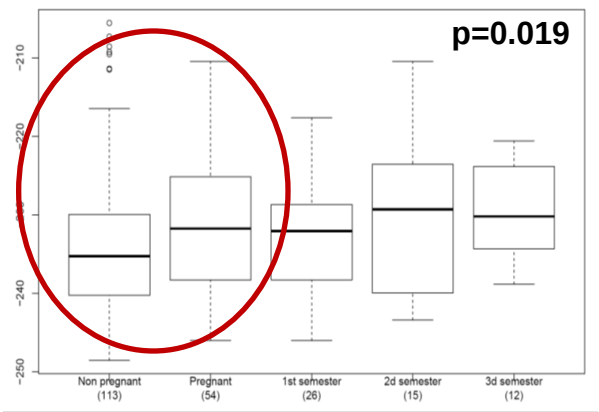
Les Amis de l'Institut Bordet

Pattern of hot spot somatic mutations in young and pregnant BC patients

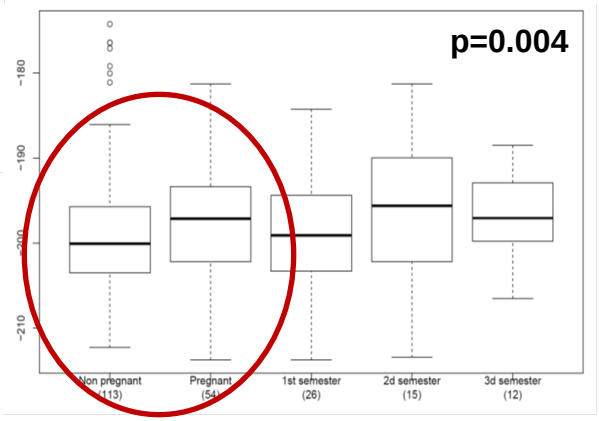
	Breast cancer patients diagnosed during pregnancy, N (%)	Breast cancer patients, not diagnosed during pregnancy, N (%)
Total number	54 (100%)	113 (100%)
PIK3CA		
- All	10 (18.6%)	26 (23%)
- Exon 9 mutations	3 (5.6%)	9 (8%)
- Exon 20 mutations	4 (7.4%)	12 (10.6%)
- Other PIK3CA mutations	3 (5.6%)	5 (4.4%)
p53	2 (3.7%)	7 (6.2%)
MAP3K1	1 (1.9%)	2 (1.8%)
STK1	1 (1.9%)	0
RET	0	1 (0.9%)

Azim HA Jr et al; Endo Rel Cancer 2014

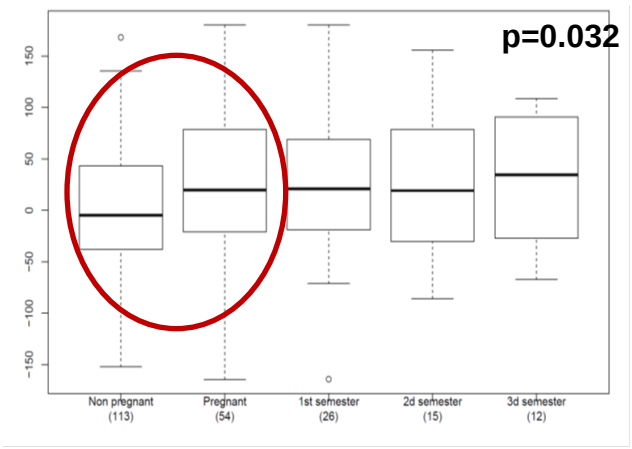
β-Catenin



SRC



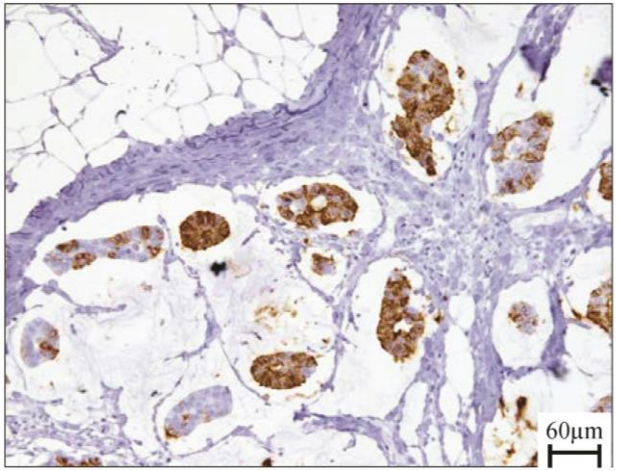
IGFR1

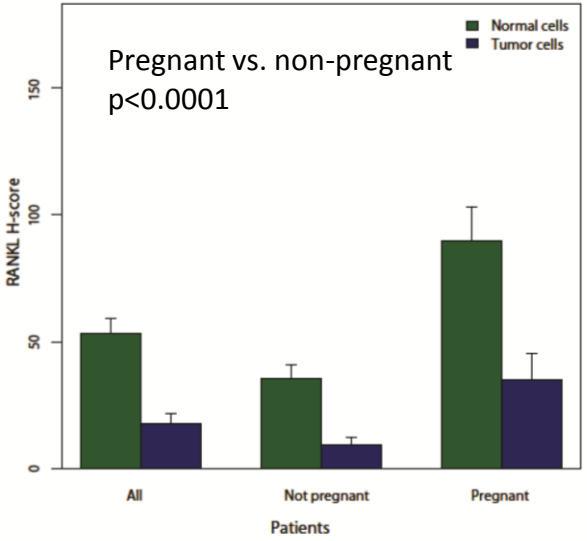


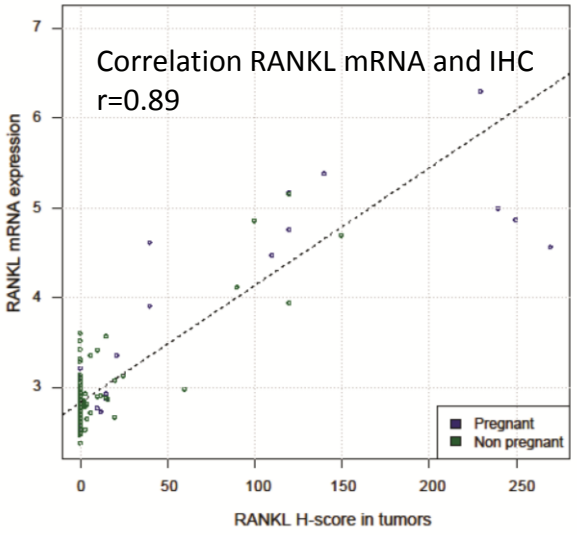
Azim HA Jr et al; Endo Rel Cancer 2014

High RANKL expression in pregnant BC patients

RANKL expression, primary tumor







In collaboration with AMGEN

esmo.org

Azim HA Jr et al; submitted

MADRID 2014 ESMO congress

VOLUME 31 · NUMBER 1 · JANUARY 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

Hatem A. Azim Jr, Niels Kroman, Marianne Paesmans, Shari Gelber, Nicole Rotmensz, Lieveke Ameye, Leticia De Mattos-Arruda, Barbara Pistilli, Alvaro Pinto, Maj-Britt Jensen, Octavi Cordoba, Evandro de Azambuja, Aron Goldhirsch, Martine J. Piccart, and Fedro A. Peccatori

Oral Presentation

EBCC 8 European Breast Cancer Conference

STATISTICS REPORT

from The 2012 European Breast Cancer Conference VIENNA

Funding

European School of Oncology

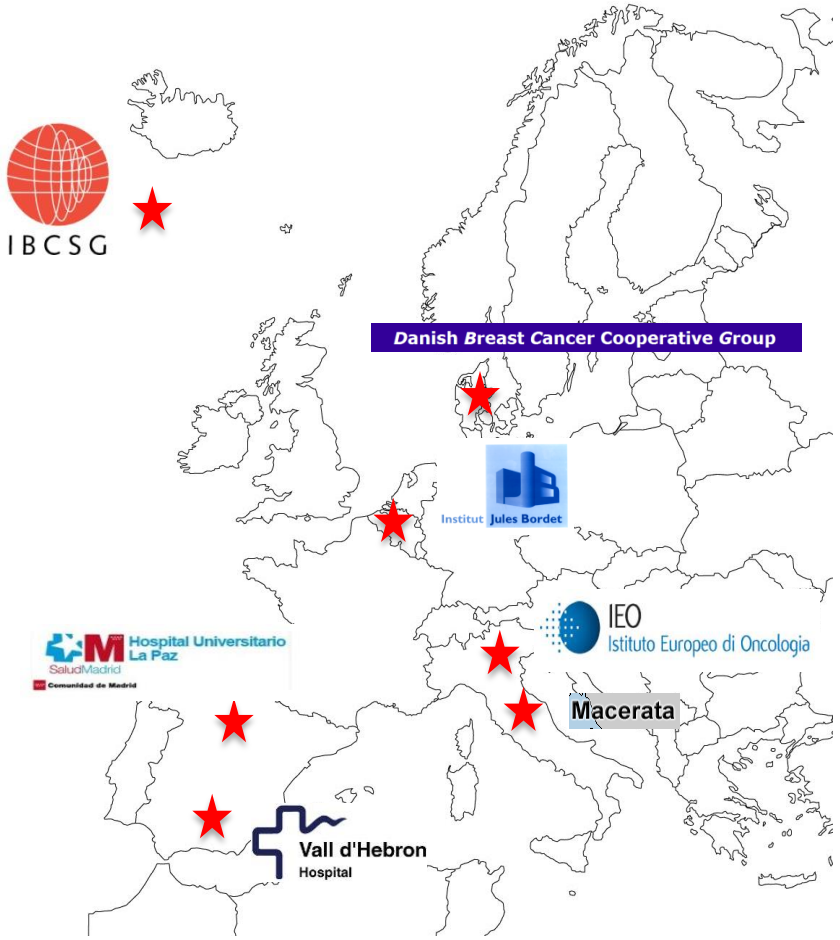
Learning to care

Les Amis de l'Institut Bordet

26-30 September 2014, Madrid, Spain

esmo.org

- Retrospective search.
- BC patients < 50 years diagnosed before 2007.
- 3 controls / pregnant case
- Confirm pregnancy status in controls.
- Unified CRF for data collection from different sites
- Data were sent to Institut Jules Bordet (IJB) for data analysis.
- Study approved by IJB Ethics committee
- STUDY POWERED TO DETECT DIFFERENCE IN DFS IN ER+ POPULATION (at least 162 ER+ pregnant women were required)



Azim HA Jr et al; JCO 2013

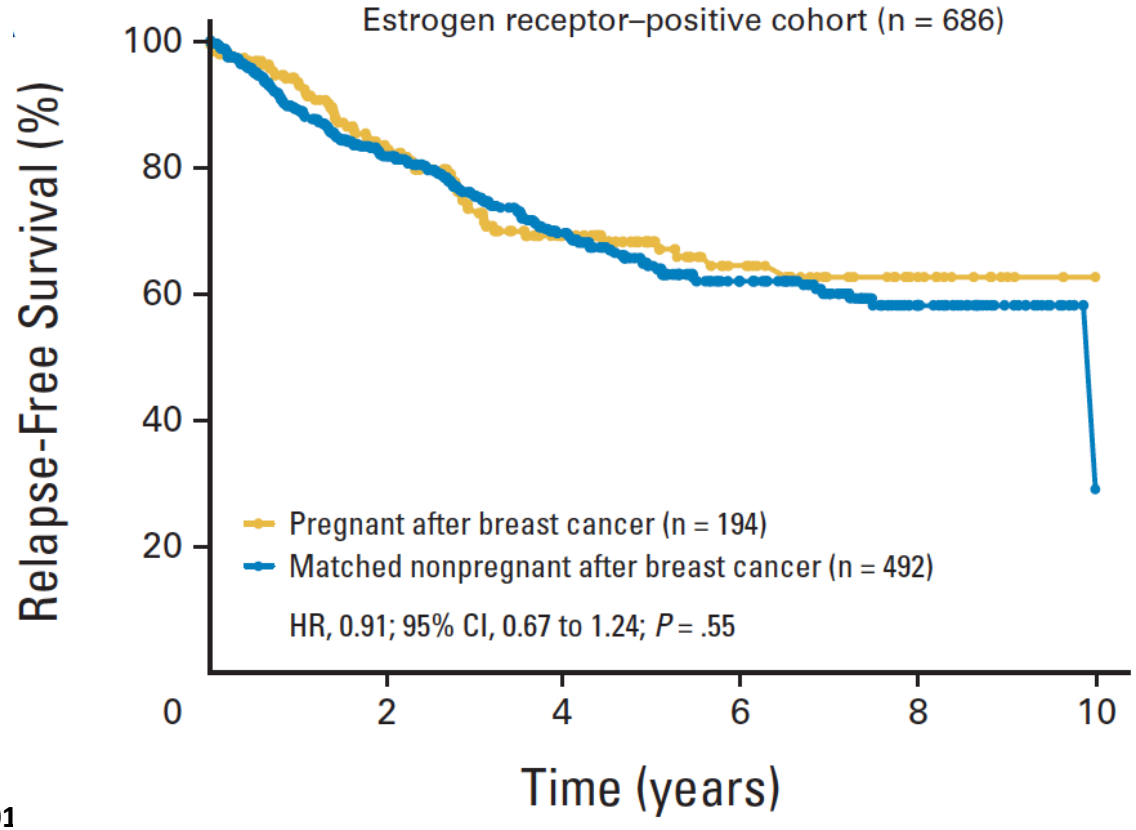
Institution/Group	Pregnant cases, n	Matched controls, n
Number	333	874
Median age (range)	31 (21-44)	34 (22-48)
Tumor size > 2cm *	135 (40.5%)	359 (41%)
Nodal status		
• Negative	188 (57%)	498 (57%)
• Positive	144 (43%)	376 (43%)
Histological grade		
• 1	37 (11%)	103 (12%)
• 2	96 (29%)	253 (29%)
• 3	114 (34%)	346 (39%)
• unknown	84 (26%)	172 (20%)
ER status		
• Negative	139 (42%)	382 (44%)
• Positive	194 (58%)	492 (56%)
Adjuvant chemotherapy received	264 (79%)	714 (82%)

* Unknown tumor size in 2% of patients;

Azim HA Jr et al; JCO 2013

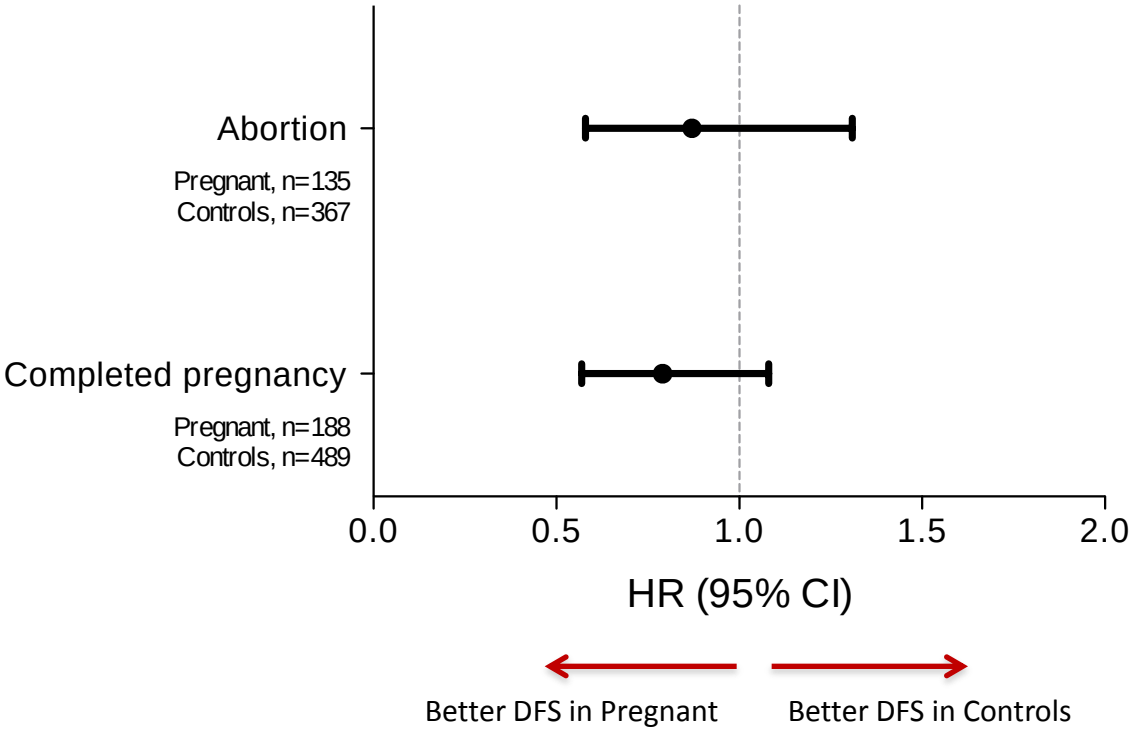
No difference in DFS in patients with ER positive disease

Median follow-up from date of conception: 4.7 years (IQR: 3.1 – 6.9)



Azim HA Jr et al; JCO 2013

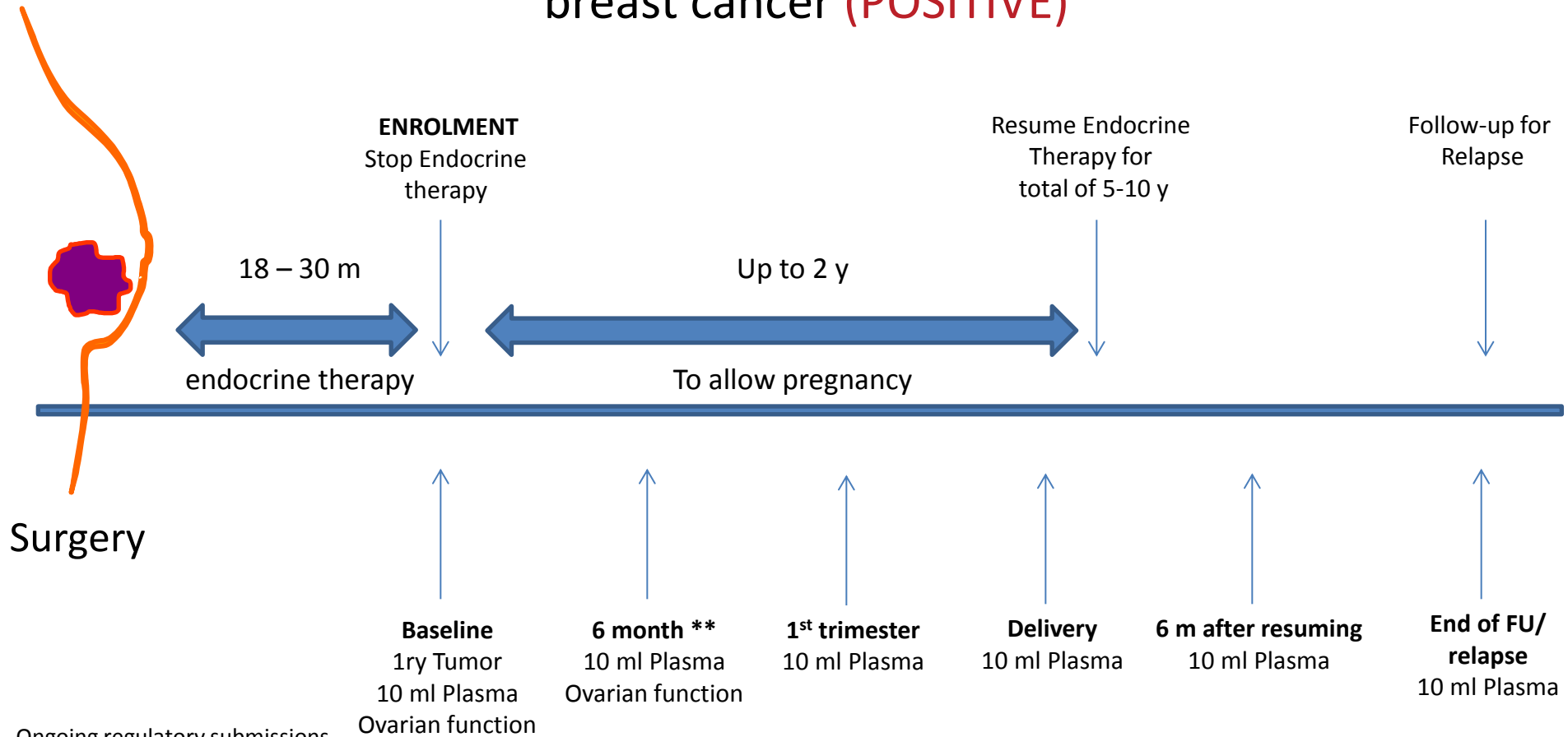
No impact of induced abortion on prognosis



Interaction test: p=0.78

Azim HA Jr et al; JCO 2013

Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine resposIVE breast cancer (POSITIVE)

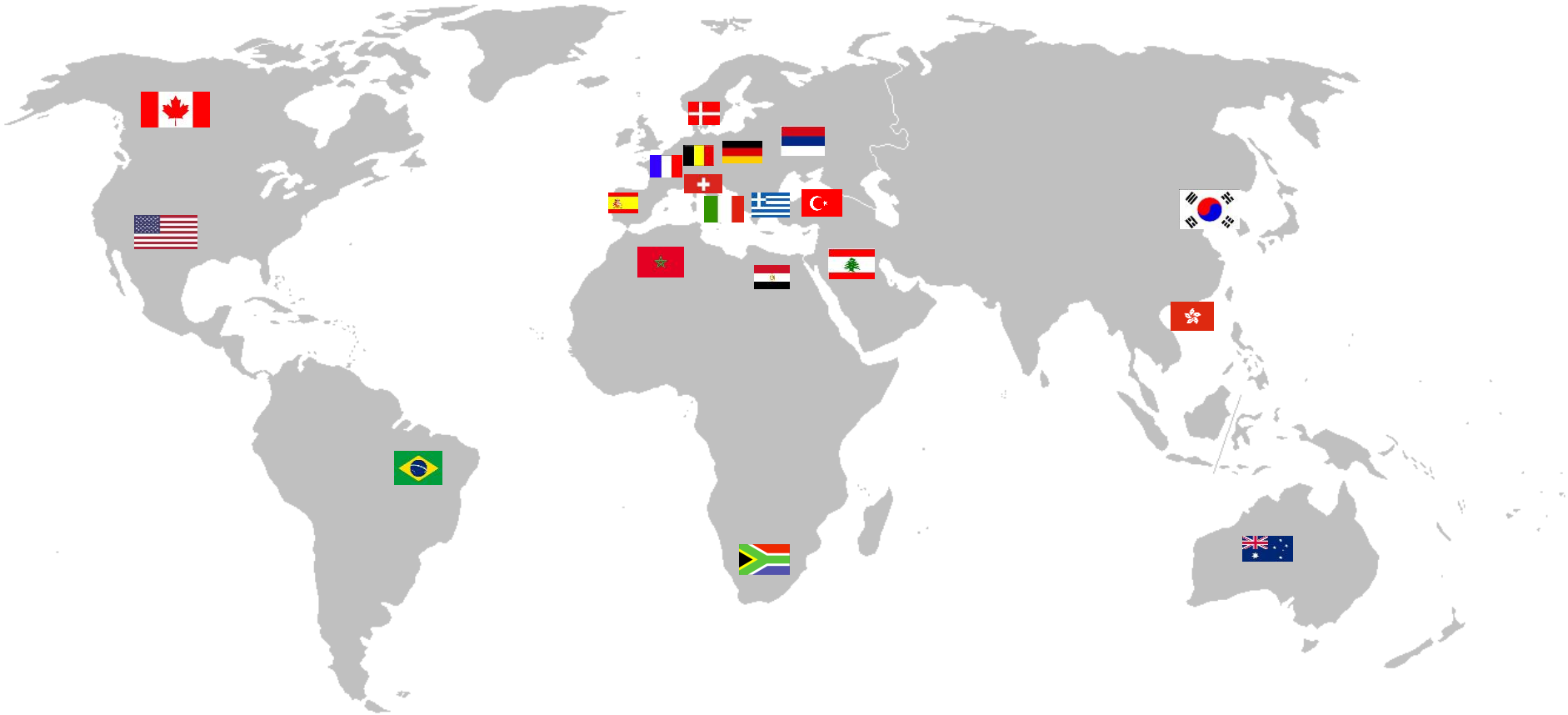


Ongoing regulatory submissions

Fellowship Outcome

MADRID 2014 ESMO congress

Extensive network +++



MADRID 2014 ESMO congress

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi160–vi170, 2013
doi:10.1093/annonc/mdt199
Published online 27 June 2013

Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. A. Peccatori[1], H. A. Azim Jr[2], R. Orecchia[3], H. J. Hoekstra[4], N. Pavlidis[5], V. Kesic[6] & G. Pentheroudakis[5], on behalf of the ESMO Guidelines Working Group*

The Breast 23 (2014) 209–220

Original article

First international consensus guidelines for breast cancer in young women (BCY1)

Ann H. Partridge [a,1], Olivia Pagani [b,c,1], Omalkhair Abulkhair [d], Stefan Aebi [e], Frédéric Amant [f], Hatem A. Azim Jr. [g], Alberto Costa [h], Suzette Delaloge [i], Gloria Freilich [j], Oreste Davide Gentilini [k], Nadia Harbeck [l], Catherine M. Kelly [m], Sibylle Loibl [n,o], Dror Meirow [p], Fedro Peccatori [h,k], Bella Kaufmann [q,2], Fatima Cardoso [r,k,*,2]

Annals of Oncology 24: 647–654, 2013
doi:10.1093/annonc/mds645
Published online 20 January 2013

Utility of prognostic genomic tests in breast cancer practice: The IMPAKT 2012 Working Group Consensus Statement†

H. A. Azim Jr[1], S. Michiels[1], F. Zagouri[2], S. Delaloge[3], M. Filipits[4], M. Namer[5], P. Neven[6], W. F. Symmans[7], A. Thompson[8], F. André[3*], S. Loi[1*] & C. Swanton[9,10]

ULB

UNIVERSITÉ LIBRE DE BRUXELLES

Membre de l'Académie universitaire Wallonie-Bruxelles

FACULTÉ DE MÉDECINE

Vu le décret du 31 mars 2004 définissant l'enseignement supérieur, favorisant son intégration dans l'espace européen de l'enseignement supérieur et refinançant les universités;

Nous, Président, Secrétaire et membres du Jury chargé de conférer le grade académique concerné, déclarons que

Hatem ABDEL AZIM

Né à CAIRE (EGYPTE), le 13 septembre 1980

a obtenu en l'année académique **2013/2014** le grade académique de

Docteur en Sciences Biomédicales et Pharmaceutiques

après défense publique d'une dissertation originale intitulée

"Breast cancer in young women: impact of pregnancy on biology and outcome"

What Am I doing now ?

Associate Director

Clinical trial unit, 75 members

breast
breast european adjuvant study team

Post-Doc

Breast Cancer Translational Research Laboratory

Medical Oncology / Data centre

M. Piccart
E. De Azambuja
A. Awada
M. Paesmans
S. Dolci

Breast Cancer Translational Research Lab

C. Sotiriou
S. Loi
M. Ignatiadis
S. Michiels
C. Desmedt
S. Brohée
S. Majjaj

Fellows

D. Fumagalli
C. Criscitiello
O. Metzger
P. Bedard
K. Saini
I. Bozovic
C. Moulin
H. Elmansy
M. Capalan

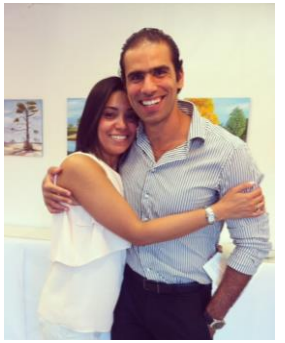
National Cancer Institute, Cairo

R. Gaafar
O. Khorshid
M. Elserafy
S. Eid
O. Mansour

Key International Collaborators

F. Peccatori
N. Pavlidis
S. Gelber
G. Pruneri
N. Kroman
O. Pagani
L. De Mattos Arruda

Funding/Research Support



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