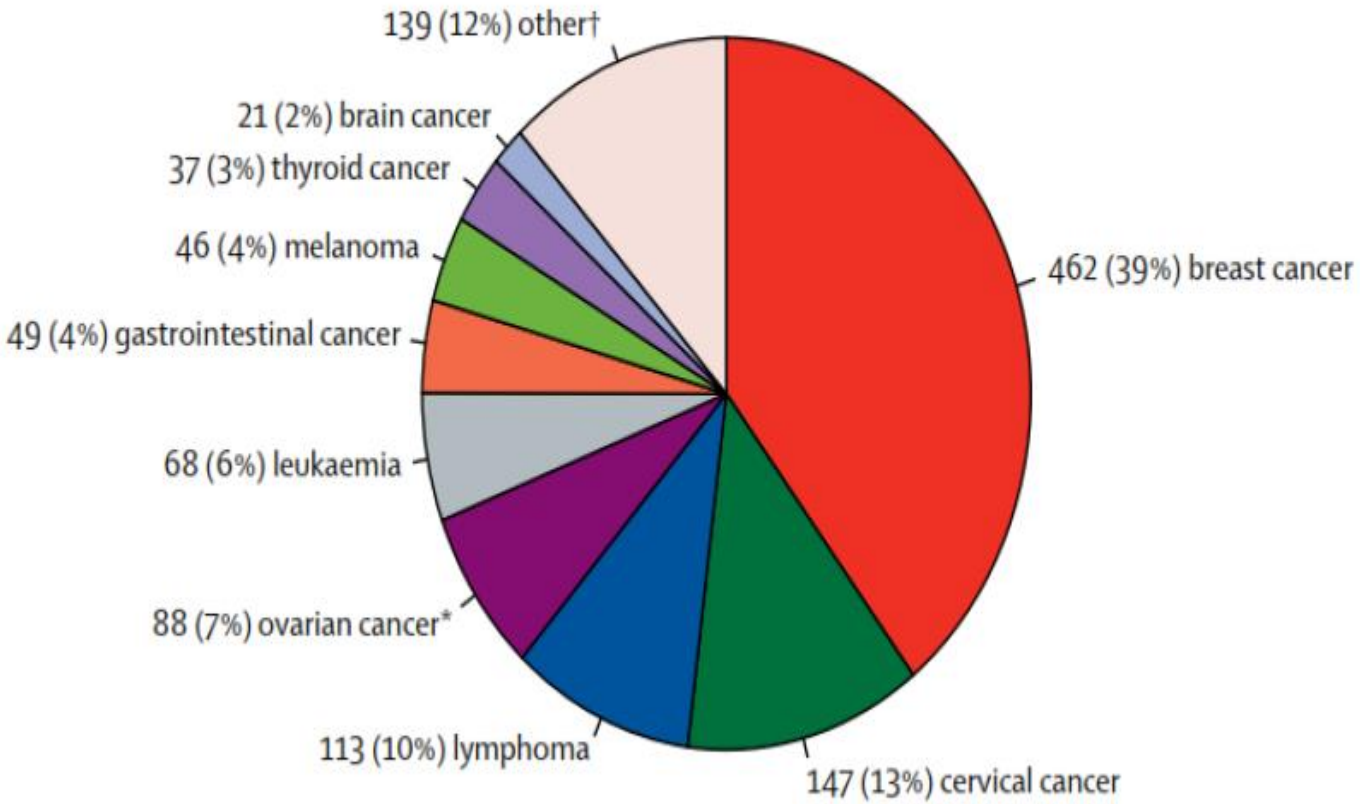
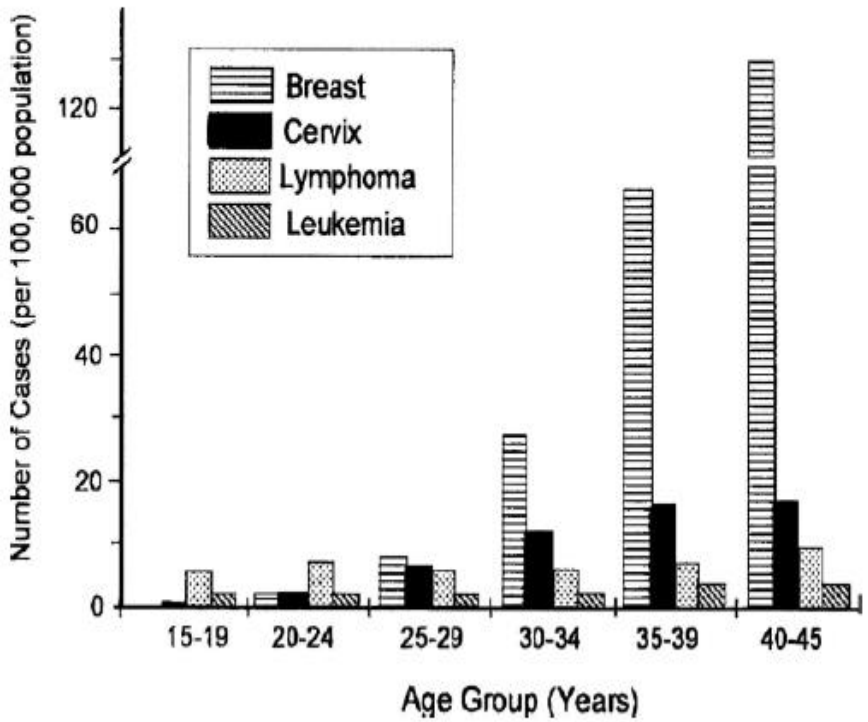
KARCINOM PRSU V TĚHOTENSTVÍ

Petra Tesařová

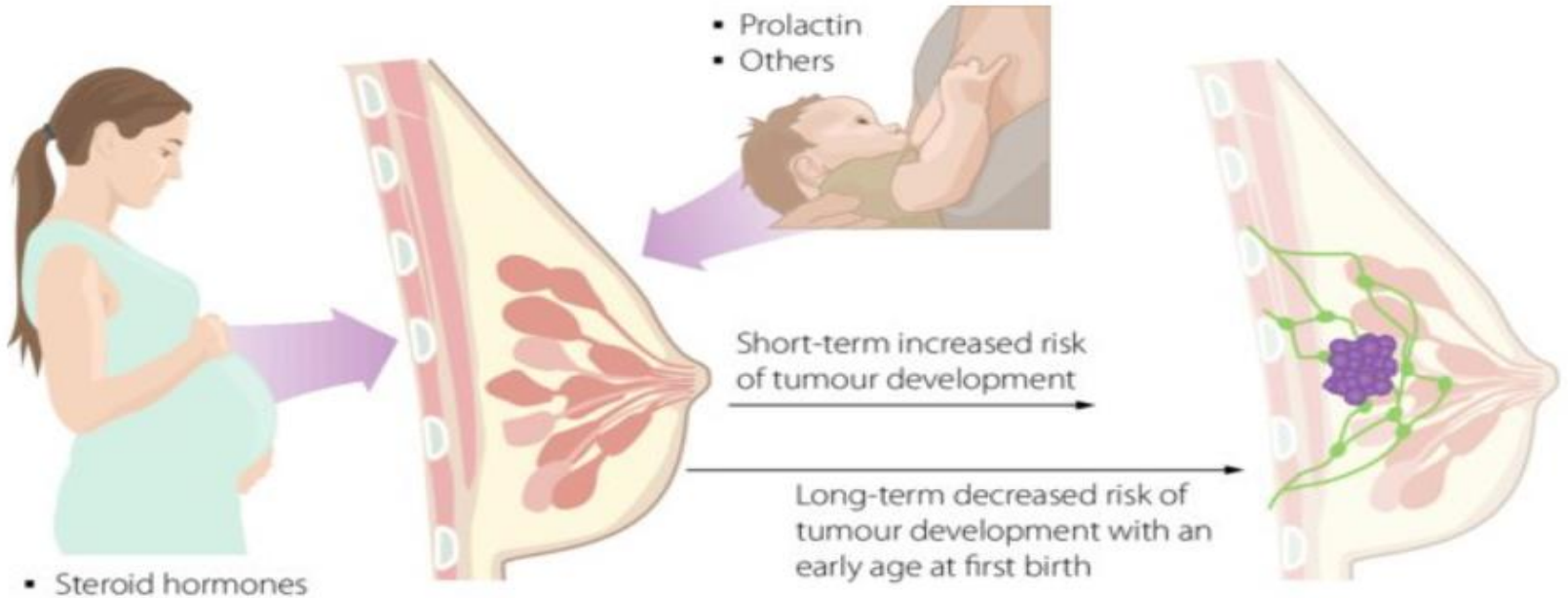
Epidemiologie





✓ 1/1000 pregnancies are complicated with cancer

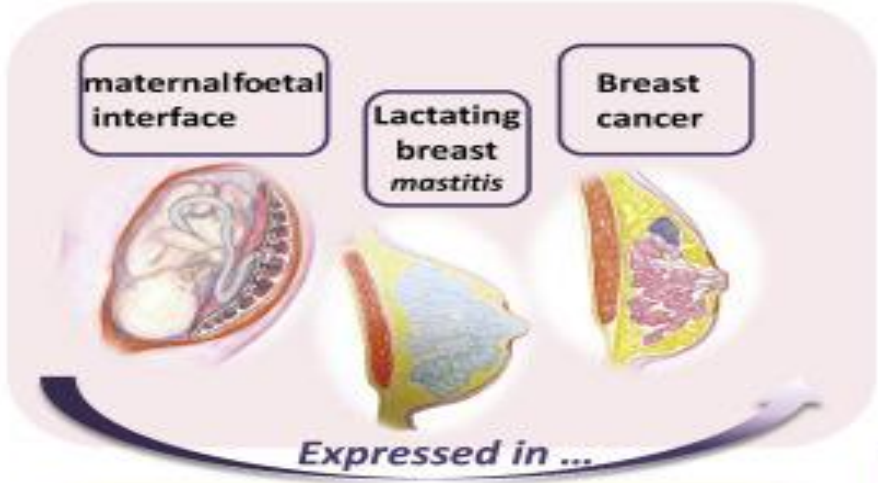
de Haan J et al, Lancet Oncol 2018
Berry et al, JCO 1999

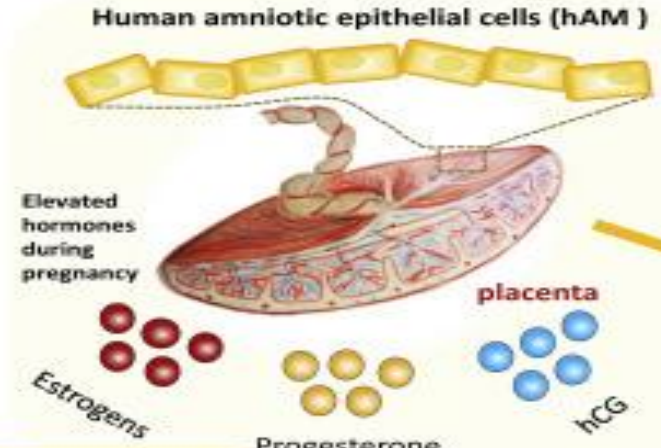


Troisi R, Bjørge T, Gissler M, et al. The role of pregnancy, perinatal factors and hormones in maternal cancer risk: a review of the evidence. *J Intern Med*. 2018;283(5):430–445. doi:10.1111/joim.12747

Pregnancy exposure to	Breast cancer	Colorectal cancer	Endometrial cancer
Excess estradiol	Increased risk	Decreased risk/ uncertain	Increased risk
Excess progesterone	Increased risk	Unknown	Decreased risk/ uncertain
Elevated levels of hCG	Decreased risk	Unknown	Unknown
Elevated levels of IGFs	Increased risk	Unknown	Unknown
Elevated levels of leptin (weight gain)	Increased risk	Unknown	Unknown

hCG, human chorionic gonadotropin; IGF, Insulin-like growth factors.





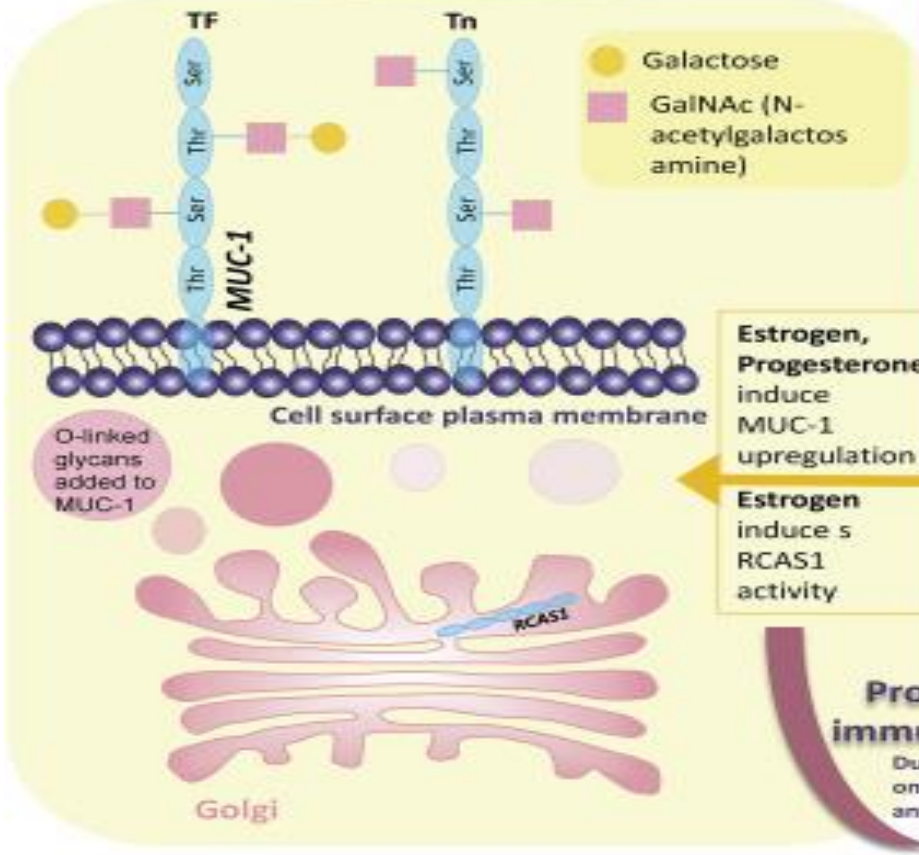
hAM: Activate apoptosis, anti-angiogenic effects

Effects of first trimester placenta:
- decrease of cancer cells in the area surrounding explants
- ER-alpha down-regulated

Non-supportive micro-environment for cancer cells

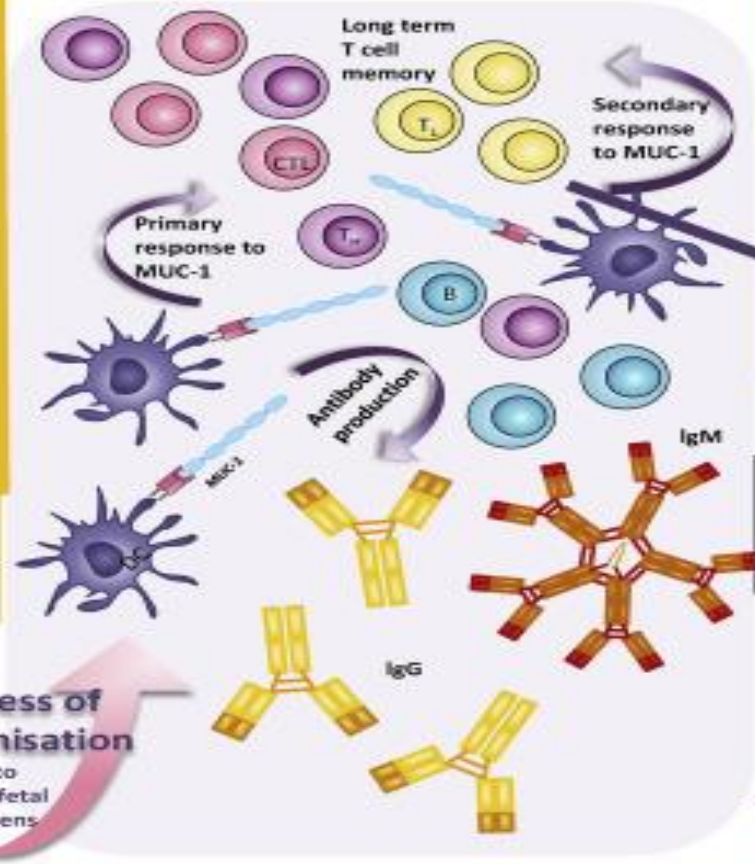
hCG: Evidence of differentiation

Protective effects on breast cancer: reduced proliferation and progression of tumours



Estrogen, Progesterone induce MUC-1 upregulation

Estrogen induce s RCAS1 activity



Factors for long term T cell memory: multiparity, lactation, mastitis

Lactation increased levels of IgG-MUC-1 significantly

Cytotoxic T / CD 8⁺ cells : Inhibit breast cancer growth

MUC-1 antibodies: Reduced risk of getting breast cancer

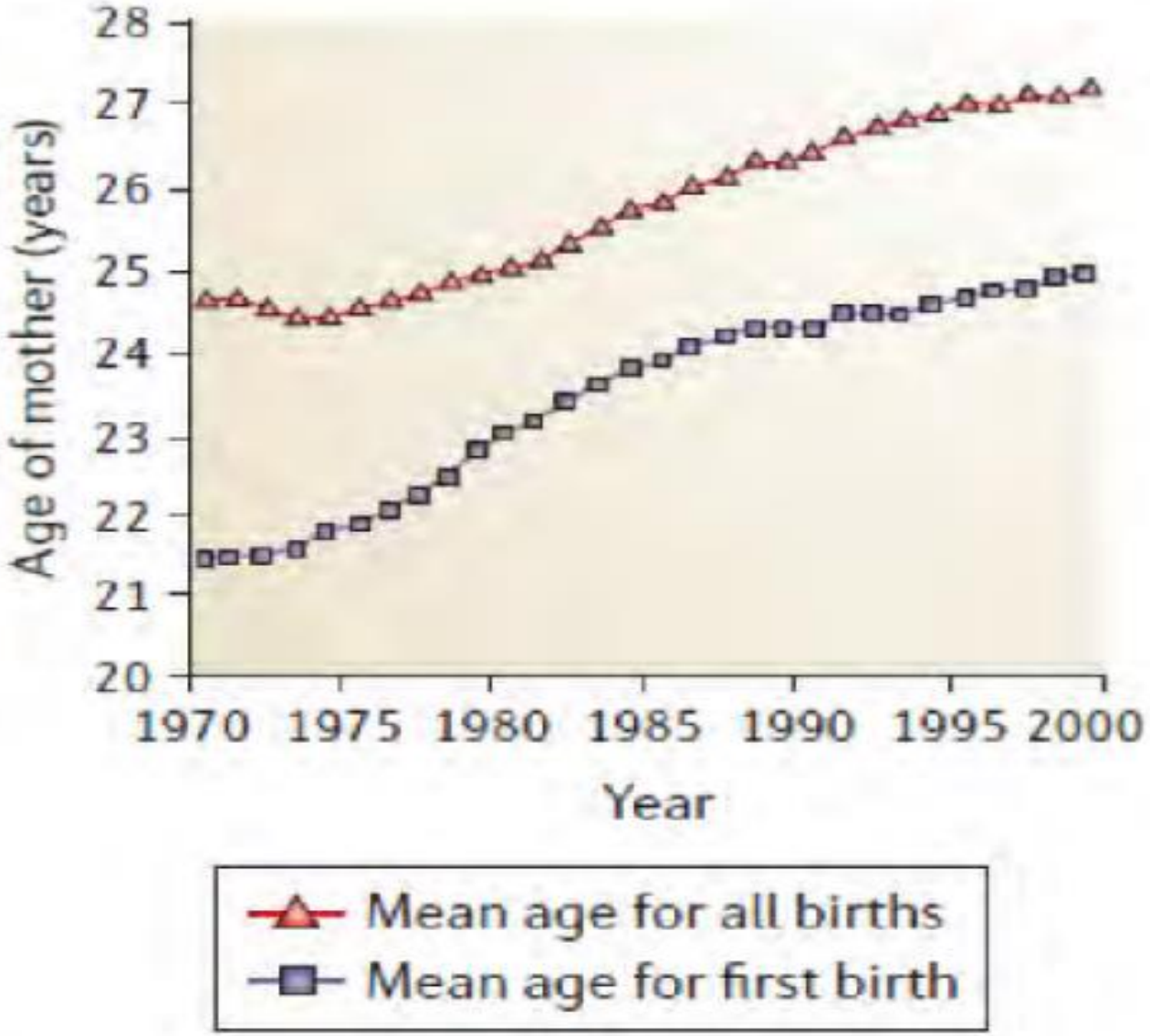
Breast cancer during pregnancy

- HER-2 overexpression
- less hormone positive tumours
- diagnosis at an advanced stage
- more aggressive subtypes

...compared to non-pregnant women

Cytotoxic T cell | T_H cell | B cell | Memory T cell

Froehlich K, EJC, 7/2019, pp 68-78



Courtesy F. Peccatori

Praha 2019 – 34 let

Prof. Pařízek

THE TOP TEN

Average age of women at birth of first child

1	UK	30
2	Germany	30
3	Italy	29.9
4	Spain	29.7
5	Switzerland	29.6
6	Luxembourg	29.3
7	South Korea	29.1
8	Japan	29.1
9	Netherlands	28.9
10	Greece	28.8
	OECD AVERAGE	27.8

Roste počet nových karcinomů prsu u mladých žen

Cancer Epidemiology 37 (2013) 544–549

Contents lists available at SciVerse ScienceDirect

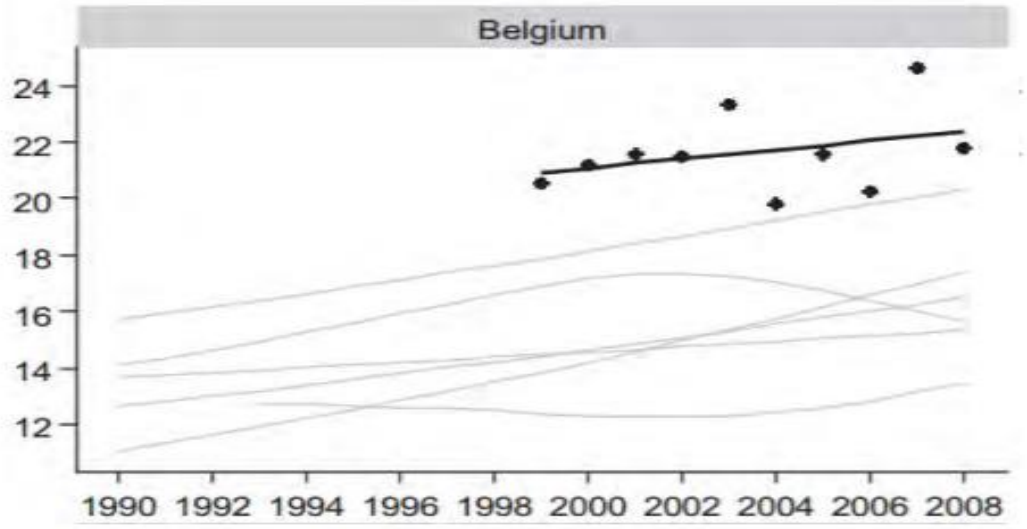
Cancer Epidemiology

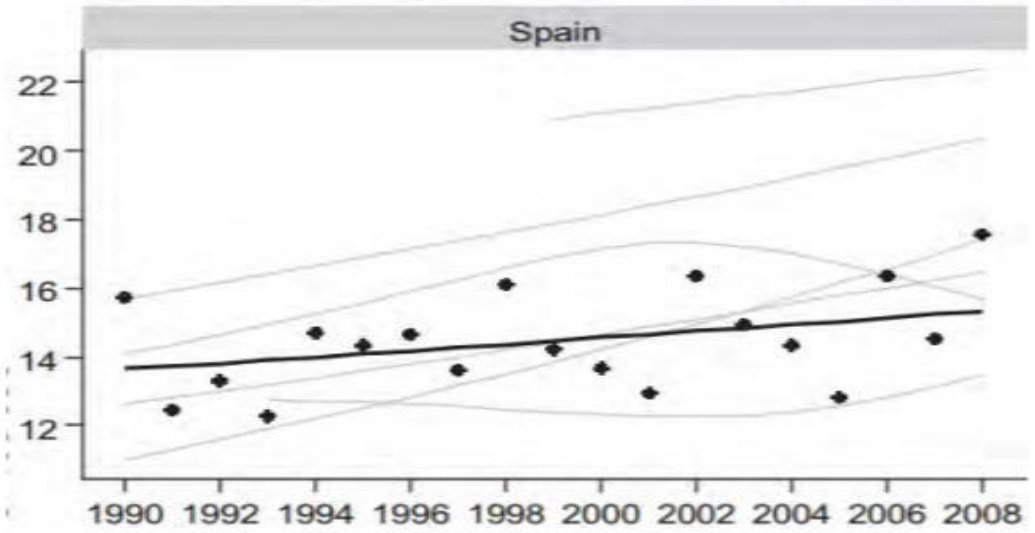
The International Journal of Cancer Epidemiology, Detection, and Prevention

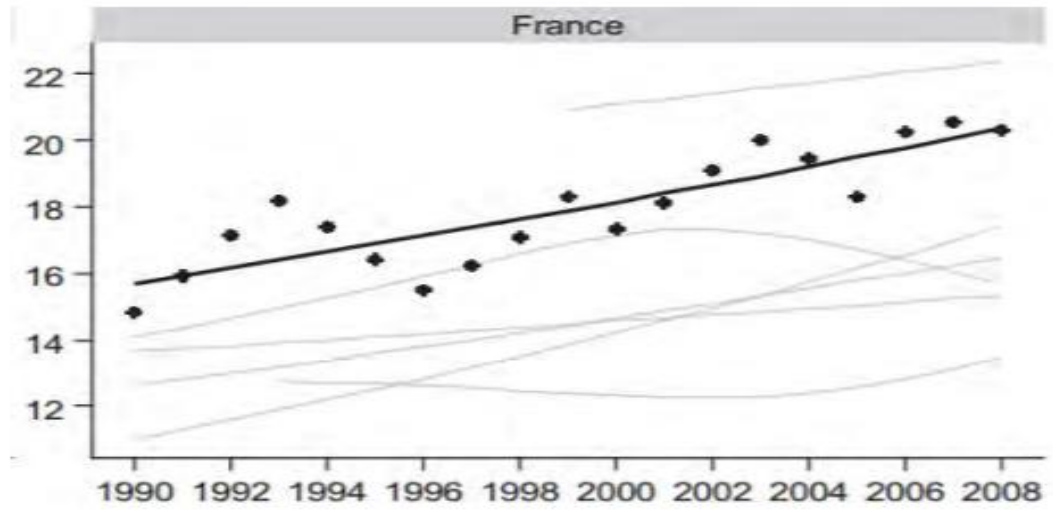
journal homepage: www.cancerepidemiology.net

Trends in incidence of breast cancer among women under 40 in seven European countries: A GRELL cooperative study

Brice Leclère [a,f,*], Florence Molinié [a,f], Brigitte Trétarre [b,f], Fabrizio Stracci [c,f], Laetitia Daubisse-Marliac [d,f], Marc Colonna [e,f]





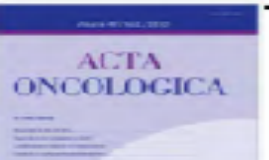


Klinická charakteristika

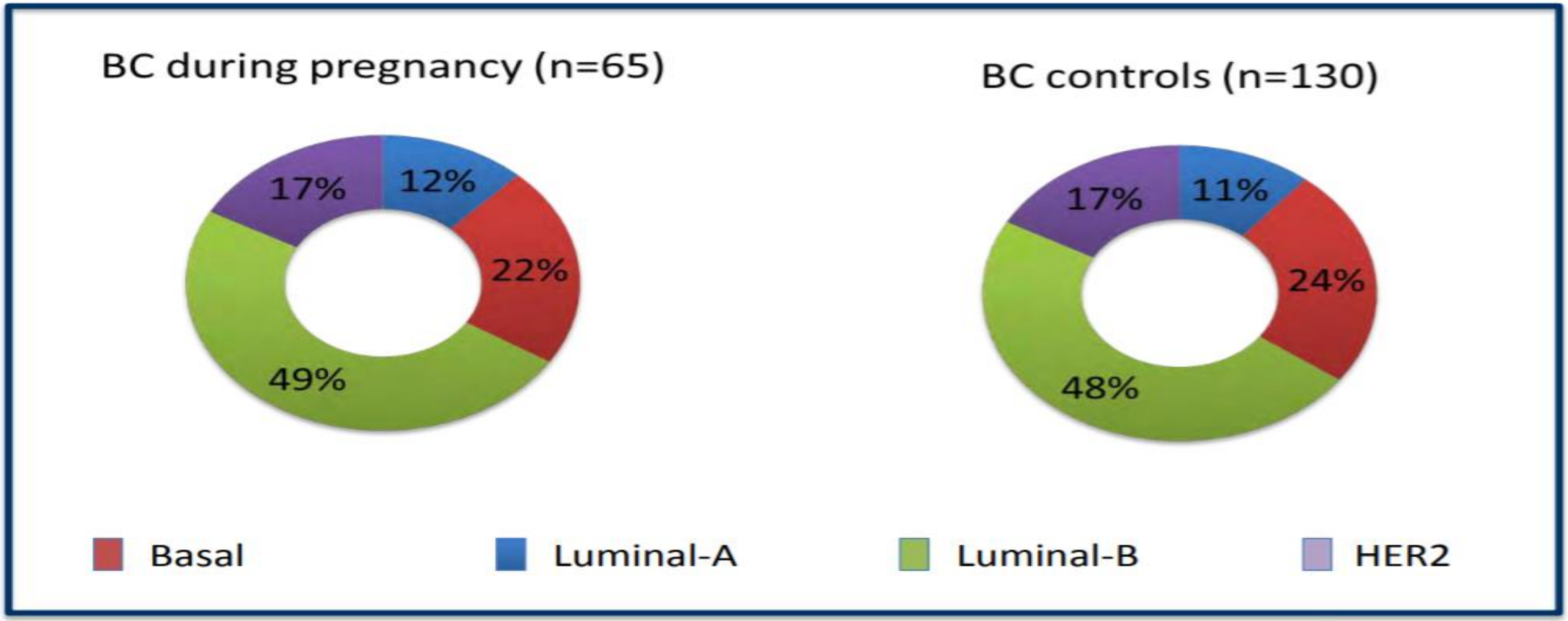
		Pregnant Cases N = 65	Controls N = 130
Age (years)	< 35	20 (30.8)	41 (31.5)
	35-39	33 (50.8)	61 (46.9)
	≥ 40	12 (18.5)	28 (21.5)
	Median	36 (28-47)	36 (28-47)
Year of Surgery	1996 - 2003	16 (24.6)	37 (28.5)
	2004 - 2005	20 (30.8)	35 (26.9)
	2006 - 2008	16 (24.6)	36 (27.7)
	2009 - 2010	13 (20.0)	22 (16.9)
	Median	2005	2005
pT	1a-b	5 (7.6)	10 (7.6)
	1c	21 (32.3)	42 (32.3)
	2	31 (47.7)	62 (47.7)
	3	6 (9.2)	12 (9.2)
	X	2 (3.1)	4 (3.1)
pN	pN0	28 (43.1)	56 (43.1)
	pN1	19 (29.2)	38 (29.2)
	pN2	10 (15.4)	20 (15.4)
	pN3	6 (9.2)	12 (9.2)
	pNx	2 (3.1)	4 (3.1)

Biologická charakteristika se příliš neliší

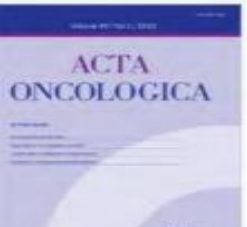
		Pregnant Cases N = 65	Controls N = 130	
Estrogen Receptor	Present	43 (66.1)	98 (75.4)	0.175
	Absent	22 (33.9)	32 (24.6)	
Progesteron Receptor	Present	42 (64.6)	87 (66.9)	0.748
	Absent	23 (35.4)	43 (33.1)	
Grade	1	4 (7.5)	4 (3.6)	0.503
	2	18 (34.0)	43 (39.1)	
	3	31 (58.5)	63 (57.3)	
Ki-67 %	< 20	18 (28.6)	30 (23.4)	0.442
	≥ 20	45 (71.4)	98 (76.6)	
Her2/neu	Negative	54 (83.1)	103 (81.1)	0.737
	Positive	11 (16.9)	24 (18.9)	
Perivascular Invasion	Absent	31 (47.7)	70 (55.1)	0.330
	Present	34 (52.3)	57 (44.9)	
Molecular subtypes	Luminal A	8 (12.3)	13 (10.3)	0.306
	Luminal B	37 (56.9)	82 (65.1)	
	Her2/Neu	6 (9.2)	4 (3.2)	
	Triple Negative	14 (21.5)	27 (21.4)	



Ani molekulární subtyp se příliš neliší



Chi-square: p=0.68



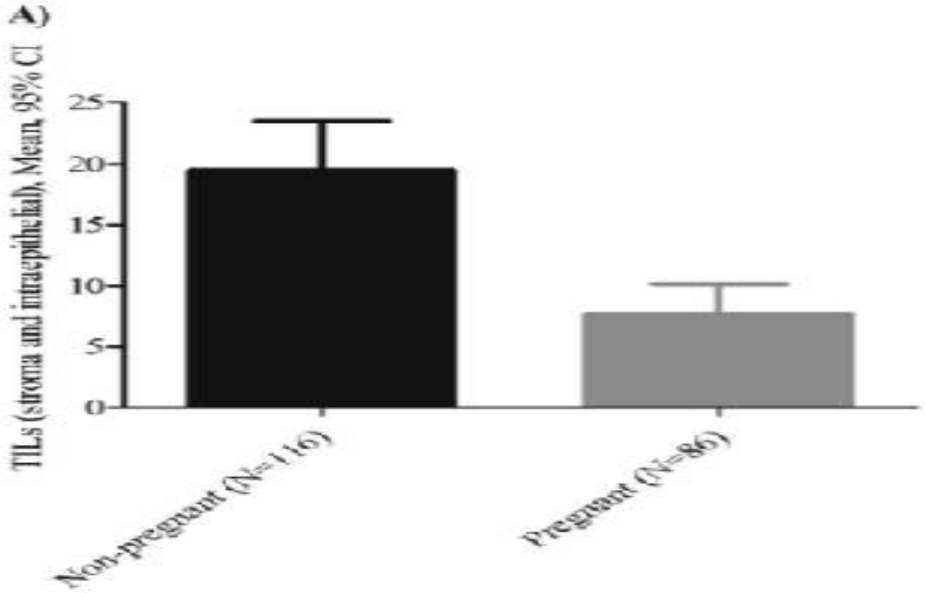
Azim HA Jr et al; Acta Oncol 2012

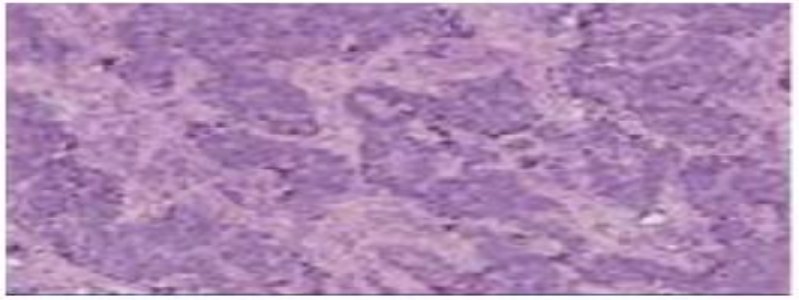
TILs je vyšší u těhotných

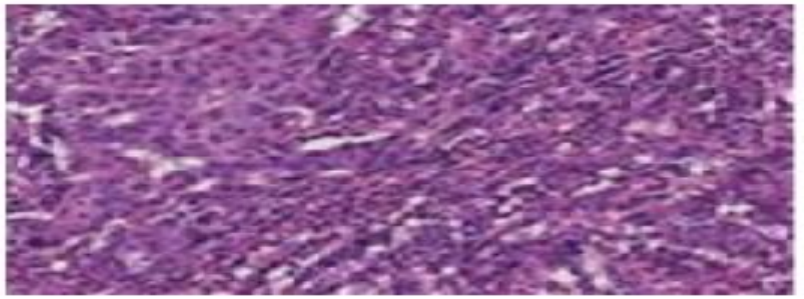
Contents lists available at ScienceDirect
The Breast
journal homepage: www.elsevier.com/brst

Tumour infiltrating lymphocytes (TILs) in breast cancer during pregnancy

Hatem A. Azim Jr. [a,*], Andrea Vingiani [b], Fedro Peccatori [c], Giuseppe Viale [b,d], Sherene Loi [c], Giancarlo Pruneri [b,d]



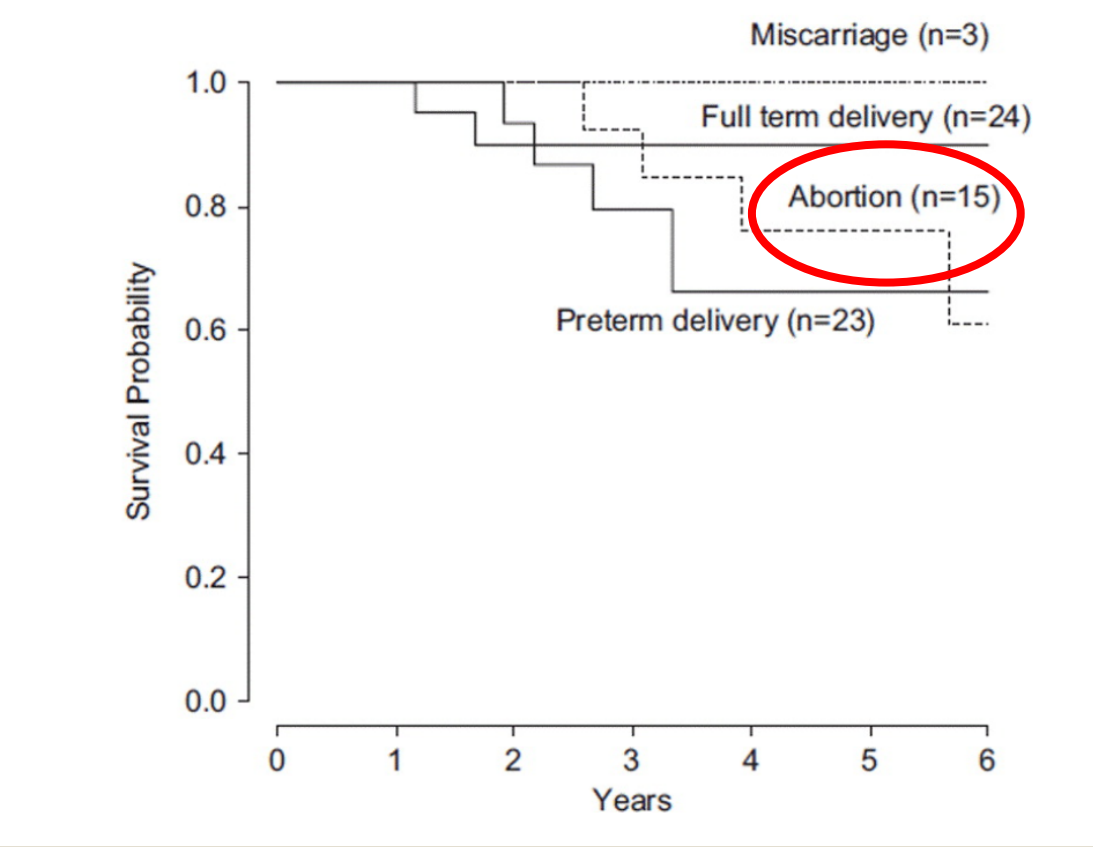




TILS ≥50%
Pregnant: 2/86 patients (2.3%)
Non-pregnant: 11/116 (9.6%), p<0.001

Léčba karcinomu prsu v těhotenství

- Měla by probíhat ve specializovaných centrech, nejlépe se zkušeností podloženou
- dostatečným množstvím léčených pacientů
- O léčbě rozhoduje multidisciplinární tým,
- jehož součástí je gynekolog – porodník
- Pacientka se musí rozhodnout zda
- v těhotenství pokračovat nebo ne
- **Interrupce neovlivňuje příznivě prognózu nemoci !**



Diagnóza

- Diagnóza rakoviny během těhotenství
- je často zpožděna
- nesprávná interpretace příznaků
- Rezistence se mění
- Podcenění nálezu
- odmítnutí pacienta
- Ultrazvukové vyšetření indikace
- Mammografie se stíněním
- MRI bez kontrastu

Staging

	Safe	Not safe
Breast	Ultrasound Mammogram	MRI with gadolinium
Chest	X-rays, Low dose CT scan (first trimester) DW-MRI*	X-rays, CT scan (beyond first trimester)
Abdomen	Ultrasound /DW-MRI*	CT scan
Bone	DW-MRI*	Bone scan
Brain	DW-MRI*	
Whole body	DW-MRI*	PET scan

* Without gadolinium

Courtesy F. Peccatori

Note: EVERYTHING THAT IS NOT INDISPENSIBLE, POSTPONE!

Original article

Whole body MRI for systemic staging of breast cancer in pregnant women

Fedro A. Peccatori [a, 1], Giovanni Codacci-Pisanelli [b, *, 1], Maria Del Grande [a], Giovanna Scarfone [c], Fabio Zugni [d], Giuseppe Petralia [e]

[a] Fertility and Procreation Unit, Department of Gynaecological Oncology, European Institute of Oncology (IEO), Milan, Italy
[b] Department of Medical and Surgical Sciences and Biotechnology, University of Rome "la Sapienza", Italy
[c] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[d] Post-graduation School in Radiodiagnostics, University of Milan, Italy
[e] Department of Radiology, European Institute of Oncology (IEO), Milan, Italy

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Keywords:
Breast cancer in pregnancy
WB-MRI in pregnancy

ABSTRACT

When breast cancer is diagnosed during pregnancy, treatment should be as close; as possible to what is used in non-pregnant patients. This requires accurate local and systemic staging: ultrasound (US) is used for local staging and allows adequate evaluation of the liver and pelvis, but chest and bones cannot be explored and imaging techniques involving exposure to ionizing radiation would be needed. However, since imaging techniques involving ionizing radiation and the use of radionuclides should be limited, whole body magnetic resonance imaging (WB-MRI) without administration of contrast agent represents a very interesting alternative, but limited data is available. In this paper we describe the obstetrical and oncological outcome of 14 patients in whom breast cancer was diagnosed during the second or third trimester of pregnancy and that were staged using WB-MRI. Median age of the patient at diagnosis was 35 years (range 20–36), median gestational age at MRI was 30 weeks (range 13–32) and median age at delivery was 38 weeks (range 32–38). At birth, one new-born presented respiratory distress syndrome and one jaundice. We conclude that diffusion-weighted MRI is feasible accurate and safe for the mother and for the foetus. It may represent the staging technique of choice in pregnant women diagnosed with breast cancer after the first trimester of pregnancy.

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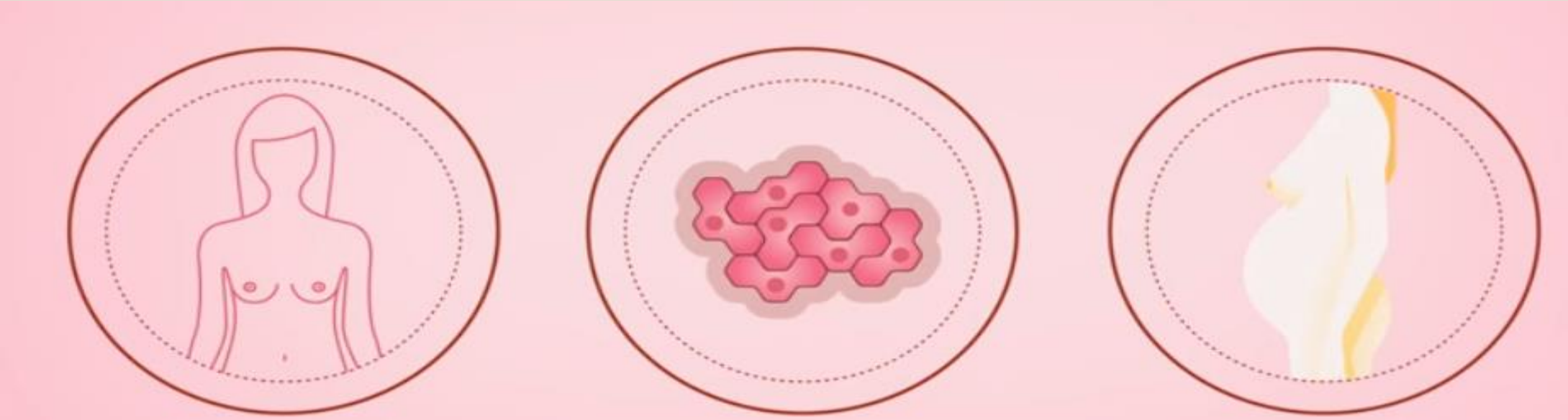
Léčebný plán



staging

typ nádoru

termín porodu

Chirurgické řešení

- Vyšší riziko potratu v 1. a na začátku 2. trimestru (RR = 1.5)

- Riziko potratu v případě chirurgického řešení mimo břišní dutinu není zvýšeno

  Možný je prs šetřící výkon i ablace
  Možná je sentinelová uzlina s izotopovým značením, ne metylenová modř.

- Monitorování krevního tlaku!
- Pečlivý anesteziologický dohled.
- Monitorování plodu.

F.Cardoso, ESMO 2019, F. Pecatori ESO YW 2018

Contents lists available at SciVerse ScienceDirect

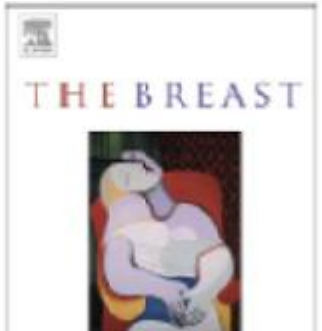
The Breast

journal homepage: www.elsevier.com/brst

Original article

Immediate breast reconstruction with expander in pregnant breast cancer patients

Visnu Lohsiriwat [a,b,1,2], Fedro Alessandro Peccatori [c,*,1,3], Stefano Martella [a,3], Hatem A. Azim Jr. [c,2], Maria Anna Sarno [c,2], Viviana Galimberti [d,3], Francesca De Lorenzi [a,3], Mattia Intra [d,3], Claudia Sangalli [e,3], Nicole Rotmensz [f,2], Giancarlo Pruneri [g,h,2], Giuseppe Renne [g,2], Mario Casales Schorr [a,3], Luiz Felipe Nevola Teixeira [i,3], Mario Rietjens [a,3], Massimo Giroda [j,3], Oreste Gentilini [d,3]



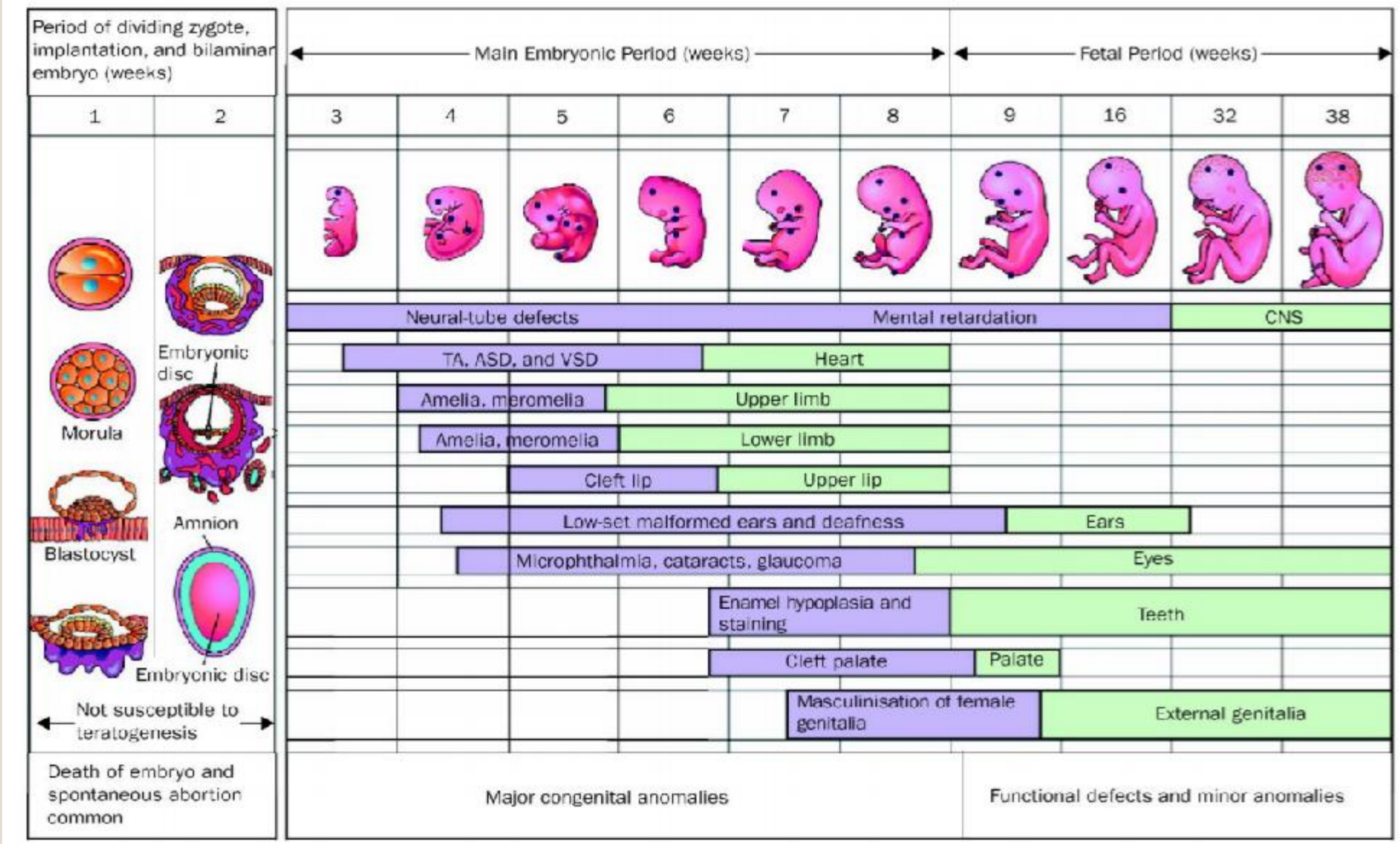
Radioterapie

F.Cardoso ESMO 2019,

- Zvýšené riziko **malformace plodu,**
- **mentální retardace** s radiační expozice> 0.1- 0.2 Gy

- Tato dávka ale není dosažena,
- pokud je RT zaměřena mimo dělohu
- (např. mozek, hlava / krk) s vhodným stíněním
-
- Nejistota ohledně **rizika malignity / sterility**
- existuje dokonce u nízkých dávek
- **Indikovat až po porodu !!!!**

Systémová léčba riziko malformací v 1.trimestru je 20%



Cardonick E & Iacobucci; Lancet Oncol 2004

Spíše sekvenčně

Dávkování podle reálné váhy

Chemoterapie

Úprava podpůrné léčby –antiemetika ano, kortikoidy a GCSF ne

Monitorace těhotenství

Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients

Jorine de Haan, Magali Verheecke*, Kristel Van Calsteren, Ben Van Calster, Roman G Shmakov, Mina Mhallem Gziri, Michael J Halaska, Robert Fruscio, Christianne A R Lok, Ingrid A Boere, Paolo Zola, Petronella B Ottevanger, Christianne J M de Groot, Fedro A Peccatori, Karina Dahl Steffensen, Elyce H Cardonick, Evgeniya Polushkina, Lukas Rob, Lorenzo Ceppi, Gennady T Sukhikh, Sileny N Han, Frédéric Amant, for the International Network on Cancer, Infertility and Pregnancy (INCIP)*

	PPROM or preterm contractions		Small for gestational age		Neonatal intensive care unit admission	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Chemotherapeutic agents	..	0·056	..	<0·0001	..	0·0086
Non-platinum alkylating (yes vs no)	2·02 (0·81–5·02)	..	2·08 (0·88–4·91)	..	0·88 (0·46–1·70)	..
Anthracyclines (yes vs no)	1·11 (0·42–2·92)	..	0·50 (0·21–1·22)	..	1·21 (0·62–2·38)	..
Antimetabolites (yes vs no)	0·89 (0·46–1·71)	..	1·24 (0·70–2·22)	..	1·03 (0·60–1·74)	..
Taxanes (yes vs no)	1·11 (0·53–2·33)	..	2·07 (1·11–3·86)	..	2·37 (1·31–4·28)	..
Platinum (yes vs no)	2·29 (0·79–6·63)	..	3·12 (1·45–6·70)	..	1·66 (0·77–3·55)	..
Other (yes vs no)	1·48 (0·61–3·63)	..	2·34 (1·04–5·25)	..	1·63 (0·78–3·38)	..

Anthracycline (N=328), Taxanes (N=84), Platinum (N=74)

Možné komplikace

	No chemotherapy during pregnancy (N=164)	Chemotherapy during pregnancy (N=179)	p value
Any obstetrical complication			
No	149 (91%)	148 (83%)	0·027
Yes	15 (9%)	31 (17%)	
Premature labour			
No	161 (98%)	169 (94%)	0·090
Yes	3 (2%)	10 (6%)	
Premature rupture of the membrane			
No	164 (100%)	174 (97%)	0·062
Yes	0 (··)	5 (3%)	
Intrauterine growth restriction			
No	163 (99%)	172 (96%)	0·069
Yes	1 (1%)	7 (4%)	

Table 4: Obstetrical complications in women with early breast cancer with and without chemotherapy during pregnancy (n=343)*

Loibl et al; Lancet Oncol 2012

Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients

Jorine de Haan, Magali Verheecke*, Kristel Van Calsteren, Ben Van Calster, Roman G Shmakov, Mina Mhallem Gziri, Michael J Halaska, Robert Fruscio, Christianne A R Lok, Ingrid A Boere, Paolo Zola, Petronella B Ottevanger, Christianne J M de Groot, Fedro A Peccatori, Karina Dahl Steffensen, Elyce H Cardonick, Evgeniya Polushkina, Lukas Rob, Lorenzo Ceppi, Gennady T Sukhikh, Sileny N Han, Frédéric Amant, for the International Network on Cancer, Infertility and Pregnancy (INCIP)*

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Platinum (yes vs no)	2·29 (0·79–6·63)	..	3·12 (1·45–6·70)	..	1·66 (0·77–3·55)	..
Other (yes vs no)	1·48 (0·61–3·63)	..	2·34 (1·04–5·25)	..	1·63 (0·78–3·38)	..

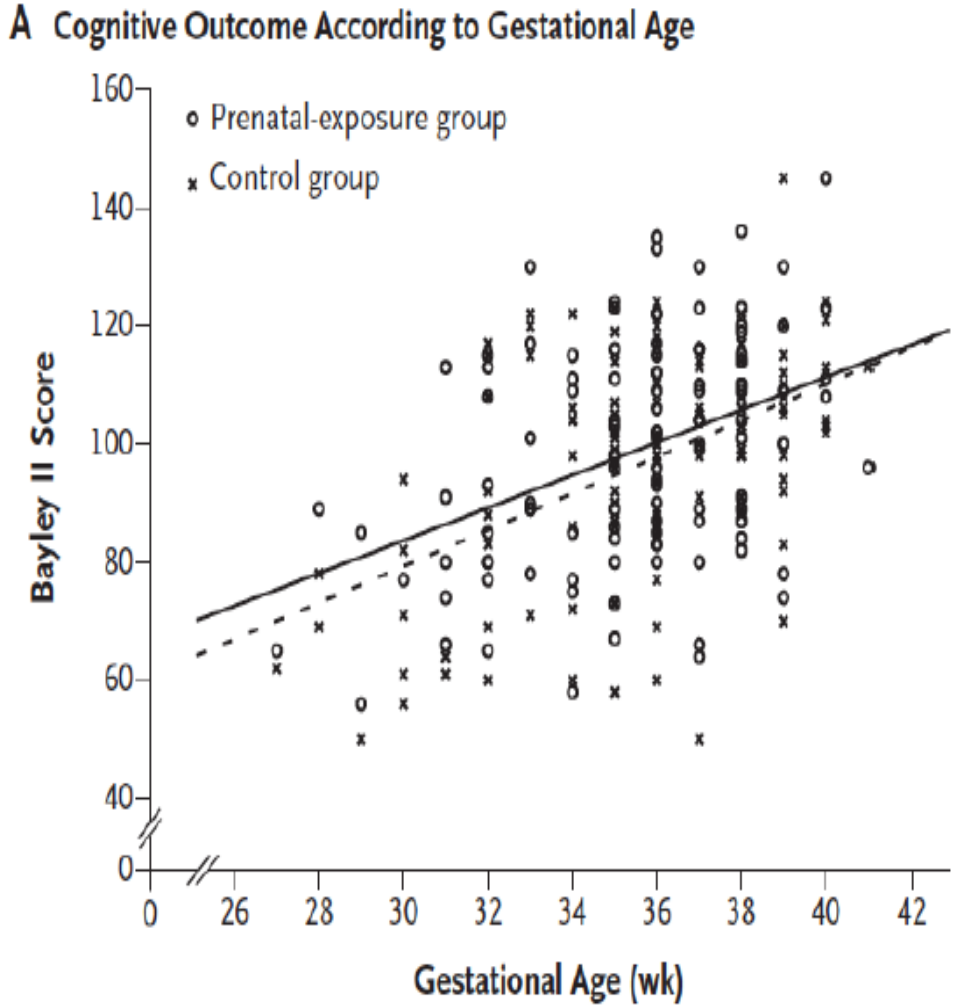
Žádný dopad na akutní úmrtnost novorozence

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy

F. Amant, T. Vandenbroucke, M. Verheecke, M. Fumagalli, M.J. Halaska, I. Boere, S. Han, M.M. Gziri, F. Peccatori, L. Rob, C. Lok, P. Witteveen, J.-U. Voigt, G. Naulaers, L. Vallaeys, F. Van den Heuvel, L. Lagae, L. Mertens, L. Claes, and K. Van Calsteren, for the International Network on Cancer, Infertility, and Pregnancy (INCIP)



Dlouhodobé kognitivní funkce souvisí s termínem porodu, nikoli v s počtem cyklů CT , Každý další měsíc těhotenství je spojen se vzestupem o 11,6 bodů v IQ koeficientu

Dopad na dítě

Peccatori Fet al, Nature RevClinOncol2015

RISK FACTORS

After gestational chemotherapy, the kids are all right

Fedro A. Peccatori, Giacomo Corrado and Monica Fumagalli

Refers to Cardonick, E. H. *et al. Am. J. Obstet. Gynecol.* http://dx.doi.org/10.1016/j.ajog.2014.11.032 (2014) | Murthy, R. K. *et al. Breast Cancer Res.* 16, 3414 (2014) | Amant, F. *et al. Lancet Oncol.* 13, 256 (2012)

When a pregnant woman is diagnosed with cancer, clinical management is complicated by concerns about the possible detrimental effects of cancer treatments on pregnancy outcome and the health of the baby. Evidence about the outcomes of children after maternal chemotherapy for cancer during pregnancy is growing and we can say 'the kids are all right'.

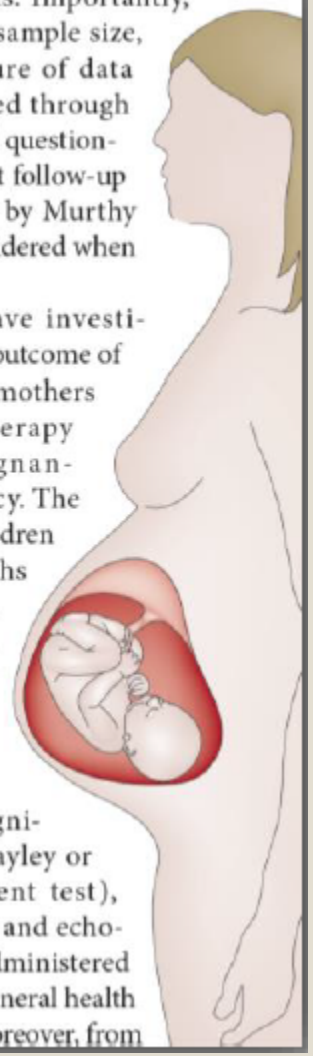
The clinical management of a pregnant woman who is diagnosed with cancer is complicated by concerns about the possible detrimental effects of oncological treatments on pregnancy outcome and the short-term and long-term health of the baby. Recent data have clarified that anthracyclines, taxanes, and platinum compounds have limited transplacental passage,[1] and when chemotherapy is administered to the pregnant woman after the first trimester, no increased risk of neonatal malformations has been described.[2] Nonetheless, concerns remain regarding the long-term health out-

> "...treating pregnant women with chemotherapy during the second or third trimester is safe..."

Recently published papers have shed light on some of these issues. Teams of researchers from the USA[6,7] and Belgium[8] have investigated the outcomes of children whose mothers had been treated with chemotherapy during pregnancy. In the study of Cardonick *et al.*,[6] 35 children who were exposed to chemotherapy during pregnancy

not jeopardize the health outcomes of the developing fetus. Importantly, however, the small sample size, the subjective nature of data acquisition (obtained through parent-administered questionnaires), and the short follow-up period in the study by Murthy *et al.*[7] should be considered when interpreting results.

Amant *et al.*[8] have investigated the long-term outcome of 70 children whose mothers received chemotherapy for various malignancies during pregnancy. The authors assessed children at birth, at 18 months of age, and at age 5–6, 8–9, 11–12, 14–15, or 18 years. They performed clinical neurological examinations, tests of the general level of cognitive functioning (Bayley or intelligence-quotient test), electrocardiography and echocardiography, and administered a questionnaire on general health and development. Moreover, from



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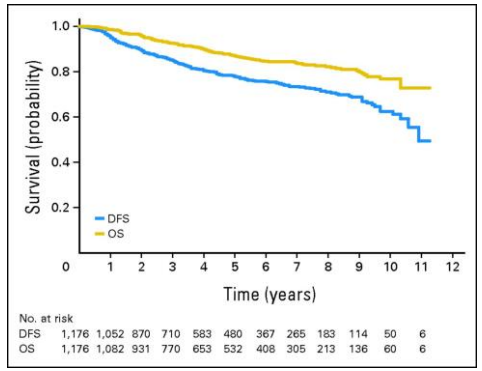
ORIGINAL REPORT

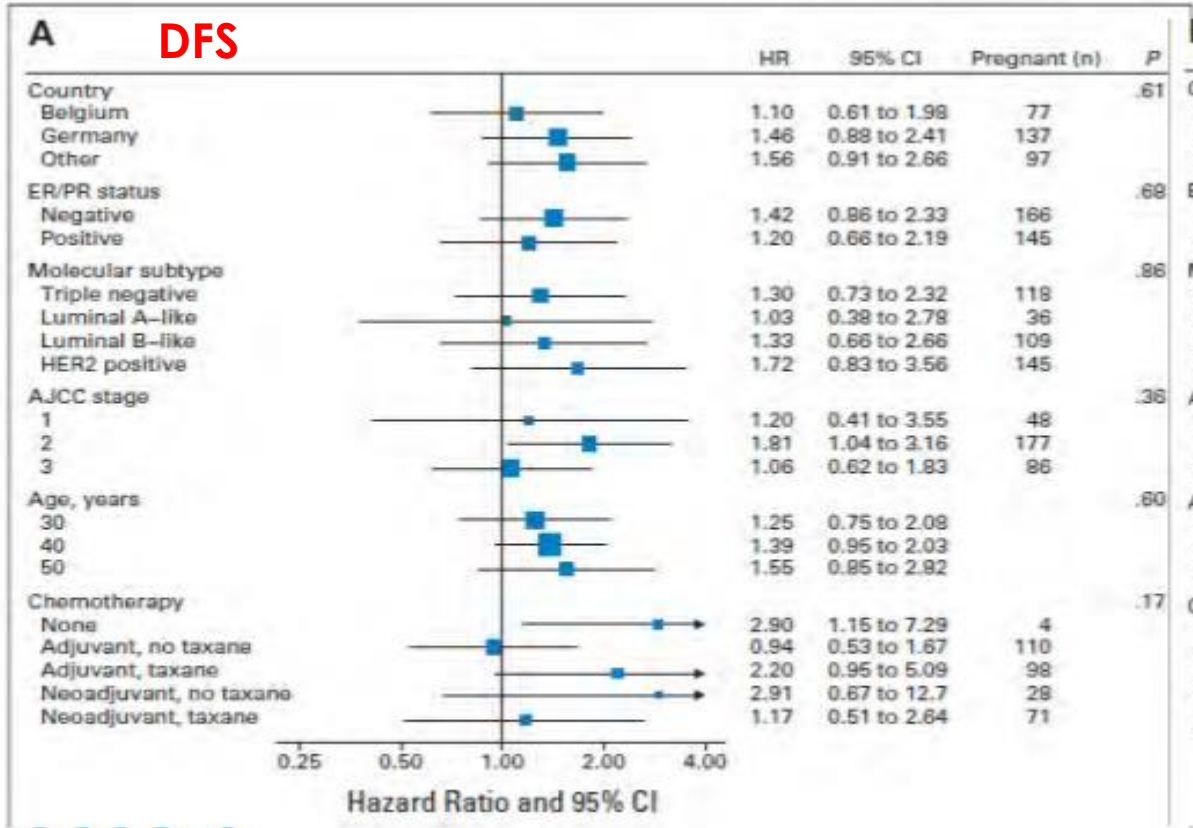
BCP Breast Cancer in

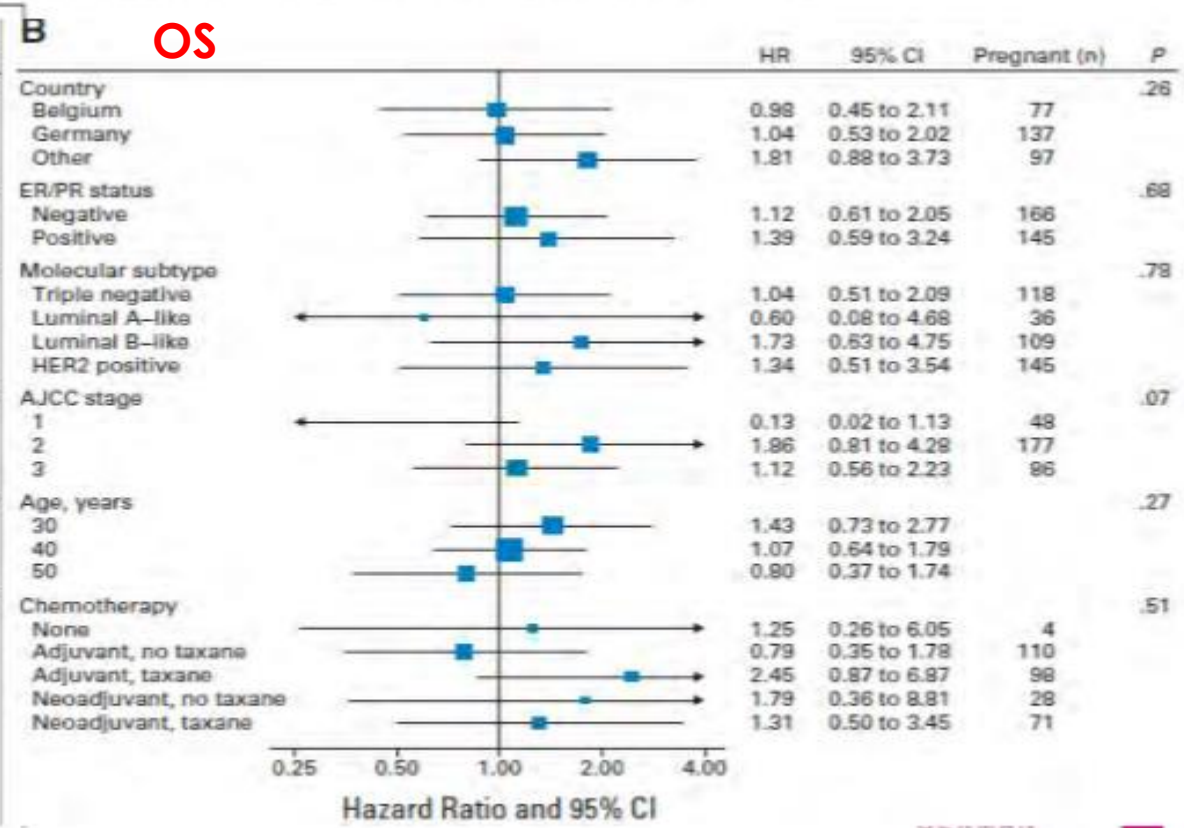


Těhotenství nezhoršuje prognózu nemocných ale.. !!!

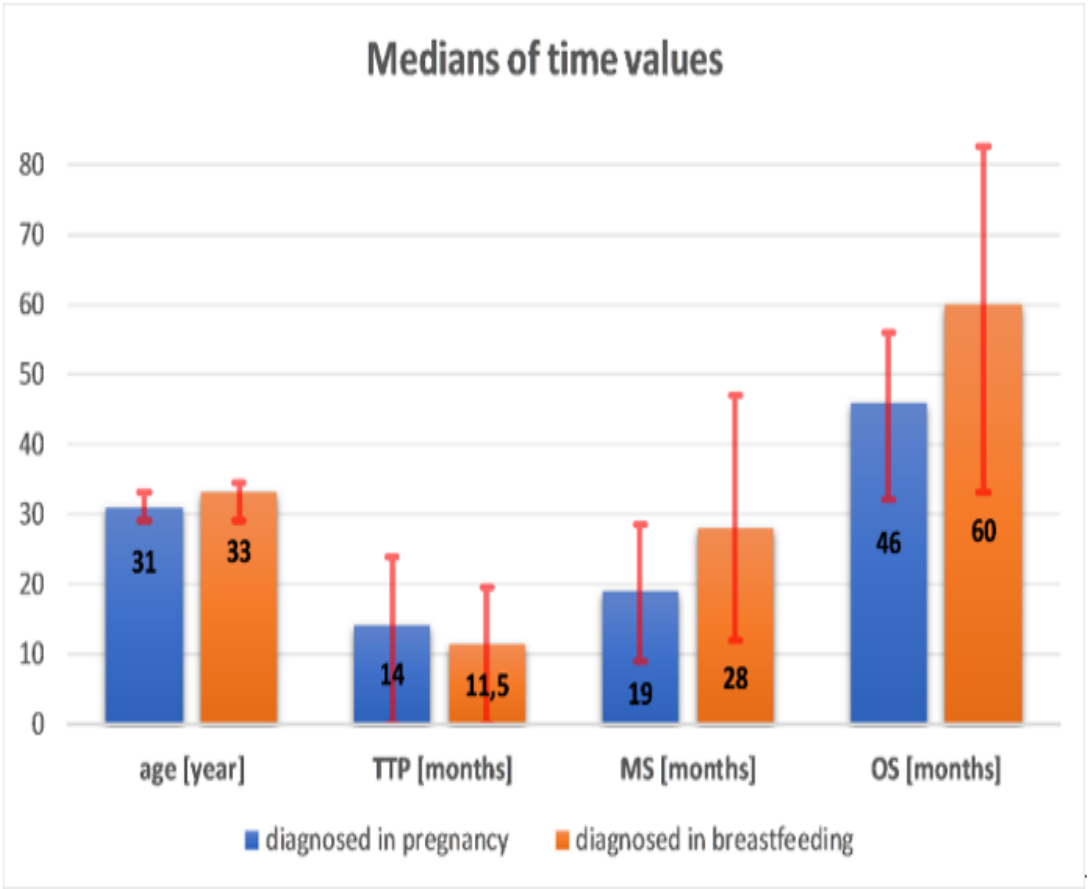
Prognosis of Women With Primary Breast Cancer Diagnosed During Pregnancy: Results From an International Collaborative Study

Frédéric Amant, Gunter von Minckwitz, Sileny N. Han, Marijke Bontenbal, Alistair E. Ring, Jerzy Giermek, Hans Wildiers, Tanja Fehm, Sabine C. Linn, Bettina Schlehe, Patrick Neven, Pieter J. Westenend, Volkmar Müller, Kristel Van Calsteren, Brigitte Rack, Valentina Nekljudova, Nadia Harbeck, Michael Untch, Petronella O. Witteveen, Kathrin Schwedler, Christoph Thomssen, Ben Van Calster, and Sibylle Loibl

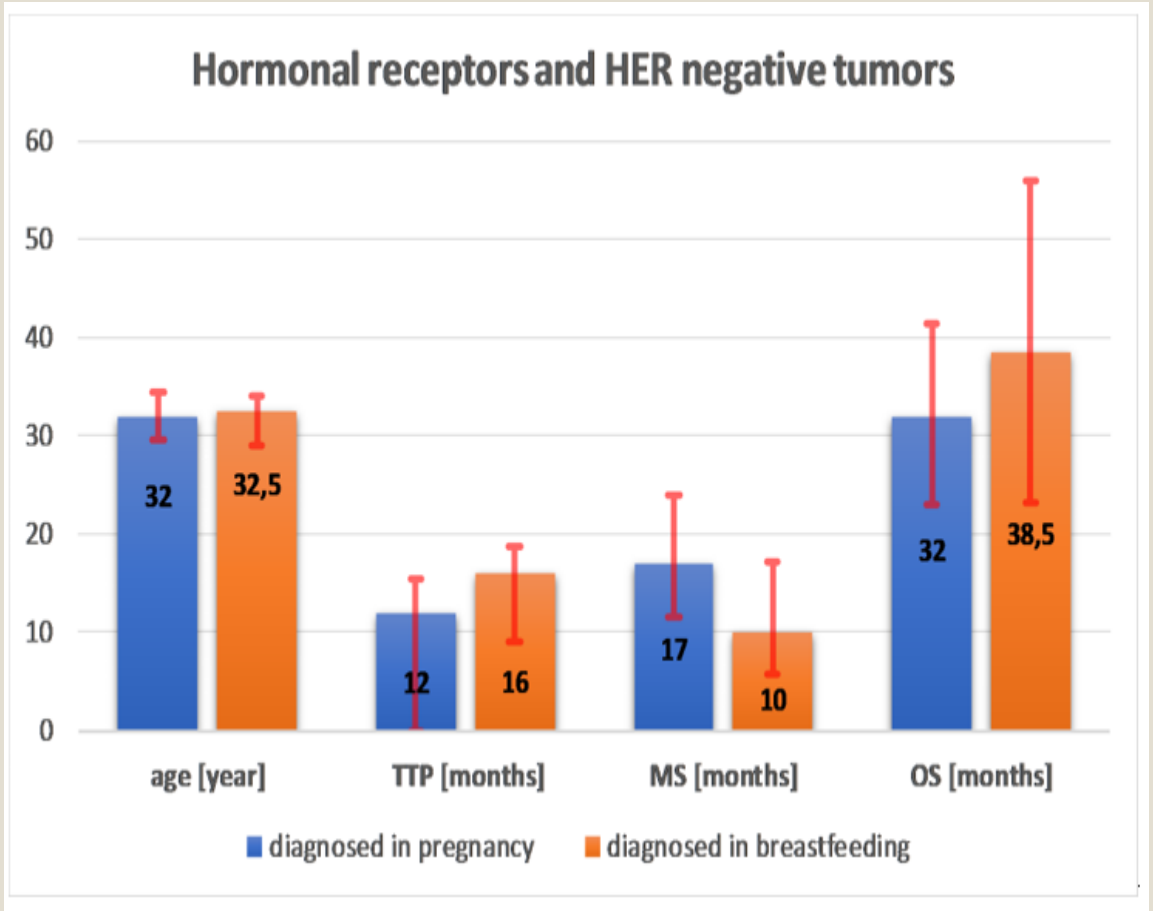




PABC



TNBC



Tesarova P, Cncers 2020 v tisku

Léčba karcinomu prsu v těhotenství

První trimestr	Druhý trimestr	Třetí trimestr	Po porodu

Radioterapie

Chirurgie prsu

Sentinelová uzlina

Chemoterapie

Chemoterapie

Hormonoterapie

Anti HER2 léčba

Vyhnout se předčasnému porodu, pokud je to možné!!!

Multidisciplinární tým

Psycholog

Rodina a přátelé