Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia Centro Oncologico ad Alta Tecnologia Diagnostica



## MELANOMA E GRAVIDANZA

### Caterina Longo

PRESIDENT



**AIDNID** 

ASSOCIAZIONE ITALIANA di DIAGNOSTICA NON INVASIVA in DERMATOLOGIA Pregnancy-associated metanoma is the most common cancer during pregnancy

31% of all cancer

with an incidence of 2.8-5 per 100 000 pregnancies

Eibye S, Kjær SK, Mellemkjær L. Incidence of pregnancy-associated cancer in Denmark, 1977–2006. Obstet Gynecol 2013

# Main questions

- diagnosis
- o scaging
- o treatment
- o prognosis



#### Nevi and pregnancy



Amy Kalowitz Bieber, BS,<sup>a</sup> Kathryn J. Martires, MD,<sup>a</sup> Marcia S. Driscoll, MD, PharmD,<sup>b</sup> Jane M. Grant-Kels, MD,<sup>c</sup> Miriam Keltz Pomeranz, MD,<sup>a</sup> and Jennifer A. Stein, MD, PhD<sup>a</sup> New York, New York; Baltimore, Maryland; and Farmington, Connecticut

#### Changes in size Key points

- Changes in the size of nevi most often occur on the front of the body, likely because of stretching of the skin during pregnancy
- Nevi on locations unaffected by skin stretching during pregnancy have not been shown to change significantly in size

JAAD 2016

Changes in the moles of pregnant women are frequently attributed to pregnancy, but recent studies suggest that pregnancy does not induce significant physiologic changes in nevi. It is common for nevi on the breasts and abdomen to grow with normal skin expansion, but studies that have examined melanocytic nevi on the backs or lower extremities have found no significant changes in size during pregnancy. Several studies have also investigated the belief that moles darken during pregnancy and have found insufficient evidence to support this idea. Dermoscopically, transient changes have been identified, but none are suggestive of melanoma. Results vary in terms of histologic changes seen in samples taken from pregnant women, but all authors agree that any histopathologic features consistent with melanoma should be viewed as melanoma and not attributed to pregnancy. Biopsy specimens should be obtained promptly from any changing mole that would raise concern for malignancy in a nonpregnant patient. Such procedures can be performed safely during pregnancy. (J Am Acad Dermatol 2016;75:661-6.)

# Main questions

- of Laghasis Scacina
- o prograosis



### Linee Guida AIOM 2017

012. La ricerca del linfonodo centinella nuò escere esequita anche in coreo di gravidanza

Qualità globale dell'evidenza	Raccomandazione clinica	Forza della raccomandazione
Molto assa	La ricerca del linfonodo sentinella può essere eseguita anche in corso di gravidanza (dopo il terzo mese di gravidanza e senza l'uso del Blu di Metilene) (105-107)	Positiva debole



I coloranti vitali come il blu di metilene hanno un basso rischio di eventi anafilattici (<1%) ma possono avere effetti teratogeni. Per tale motivo se ne sconsiglia l'utilizzo in gravidanza.

Gli autori raccomandano di spiegare attentamente rischi e benefici alle pazienti prima del trattamento.

Gentilini O et al (106) hanno valutato retrospettivamente 12 donne sottoposte in gravidanza a SLNB per carcinoma mammario.

La metodica ha permesso di identificare due pazienti portatrici di metastasi linfonodale favorendone il microstaging accurato.

Nessuna complicanza è stata rilevata; un bambino è stato sottoposto alla nascita a riparazione cardiochirurgia di un difetto interatriale che era già stato rilevato da un ECO morfologica eseguita prima della linfoscintigrafia. Anche questi autori sottolineano la fattibilità e la sicurezza della metodica.

Broer N. et al (107), diversamente, sconsigliano l'esecuzione della procedura in gravidanza riportando la loro esperienza: 5 pazienti trattate per melanoma asportando il primitivo in anestesia locale e rimandando il completamento del trattamento chirurgico al termine della gravidanza. Gli autori si riferiscono ad una Review del 2005 di Cohen-Kerem et al (108) che aveva evidenziato il rischio sulla gravidanza dell'anestesia generale: 5,8% di aborti spontanei e 3,5% di nascite premature. Questa revisione tuttavia si riferisce ad interventi non ginecologici (tra questi molta chirurgia maggiore) eseguiti anche al primo trimestre di gravidanza e quindi con risultati non pertinenti.

Il blu di metilene è considerato teratogeno e pertanto non dovrebbe essere utilizzato in gravidanza per la ricerca del linfonodo sentinella (109)

Queste casistiche sono in ogni caso limitate per la scarsa numerosità dei pazienti e il carattere retrospettivo della casistica.

#### **ORIGINAL ARTICLE**

# Pregnancy and melanoma: a European-wide survey to assess current management and a critical literature overview

S. Ribero, <sup>1,2,\*,†</sup> C. Longo, <sup>3,†</sup> E. Dika, <sup>4</sup> C. Fortes, <sup>5</sup> S. Pasquali, <sup>6</sup> E. Nagore, <sup>7</sup> D. Glass, <sup>1</sup> C. Robert, <sup>8</sup> A.M. Eggermont, <sup>8</sup> A. Testori, <sup>9</sup> P. Quaglino, <sup>2</sup> P. Nathan, <sup>10</sup> G. Argenziano, <sup>11</sup> S. Puig, <sup>12</sup> V. Bataille, <sup>13</sup>

#### **Abstract**

**Background** Management of melanoma during pregnancy can be extremely challenging. The reported incidence of melanoma in pregnancy ranges from 2.8 to 5.0 per 100 000 pregnancies. There are no guidelines for the management of melanoma during pregnancy.

**Methods** The survey was designed to investigate the opinions of melanoma physicians on decision making in relation to pregnancy and melanoma. A clinical scenario-based survey on management of pregnancy in melanoma was distributed all over Europe via the membership of the EORTC and other European melanoma societies.

**Results** A total of 290 questionnaires were returned with a larger participation from southern Europe. A large heterogeneity was found for the answers given in the different clinical scenarios with 50% of the answers showing discordance, especially regarding sentinel lymph node biopsy during pregnancy. Discordant answers were also found for the counselling of women about a potential delay in getting pregnant after a high-risk melanoma (35% for a 2 year wait minimum vs. 57% no waiting needed), while for thin melanomas, as expected, there was more concordance with 70% of the physicians recommending no delay. Fifteen per cent of physicians recommended an abortion in stage II melanoma during the third month of pregnancy. Twenty per cent of the responders advised against hormonal replacement therapy in melanoma patients.

**Conclusions** The management of melanoma during pregnancy varies widely in Europe. At present, there is a lack of consensus in Europe, which may lead to very important decisions in women with melanoma, and guidelines are needed. Received: 16 October 2015; Accepted: 18 January 2016

#### **ORIGINAL ARTICLE**

# Pregnancy and melanoma: a European-wide surve assess current management and a critical literatur overview

S. Ribero, 1,2,\*,† C. Longo, 3,† E. Dika, 4 C. Fortes, 5 S. Pasquali, 6 E. Nagore, 7 D. Glass, 1 C. Ro A.M. Eggermont, 8 A. Testori, 9 P. Quaglino, 2 P. Nathan, 10 G. Argenziano, 11 S. Puig, 12 V. Ba Members of the Melanoma Group of the EORTC

1 December 1 of Train Bosonial Continue Friday in Landon Live College Landon Landon Live College Landon Landon Live College Landon Landon Live College Landon Landon

physicians recommending no delay. Fifteen per cent of physicians recommended an abortion in stage II melanoma during the third month of pregnancy. Twenty per cent of the responders advised against hormonal replacement therapy in melanoma patients.

**Conclusions** The management of melanoma during pregnancy varies widely in Europe. At present, there is a lack of consensus in Europe, which may lead to very important decisions in women with melanoma, and guidelines are needed. Received: 16 October 2015; Accepted: 18 January 2016

# Main questions

- o diaghosis
- 6 Elminitari
- prognosis

## Does pregnancy influence melanoma prognosis? A meta-analysis

Athanassios Kyrgidis<sup>a</sup>, Aimilios Lallas<sup>a</sup>, Elvira Moscarella<sup>a</sup>, Caterina Longo<sup>a</sup>, Roberto Alfano<sup>b</sup> and Giuseppe Argenziano<sup>c</sup>

Melanoma Res 2017

The literature has not been able to conclude whether pregnancy influences the prognosis of melanoma. The aim of this study was to explore the prognosis of melanoma diagnosed during pregnancy or post partum [pregnancyassociated melanoma (PAM)] compared with melanoma in female patients who were not pregnant. We systematically searched for studies of female patients with melanoma tha reported outcomes related to survival Fifteen eligible studies were found. Overall, PAM was associated with a 17% higher mortality compared with melanoma diagnosed in female patients who were not pregnant (hazard ratio = 1.17, 95% confidence interval: 1.03–1.33, P = 0.02). The heterogeneity associated with this test was moderate  $(P = 0.07; I^2 = 38\%)$ . PAM was also associated with a 50% higher recurrence rate compared with melanoma not associated with pregnancy (hazard ratio = 1.50, 95% confidence interval: 1.19-1.90, P < 0.001). The heterogeneity associated with this test was low (P = 0.69;  $I^2 = 0\%$ ). A limitation of this meta-analysis is the definition of PAM. which is not unanimous among the studies included. Our

Fig. 2

Study or Subgroup	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95%	CI		d Ratio  , Fixed, 95% Cl	
Daryanani 2003	2.3%	0.73 [0.31, 1.70	0]	_		
Johansson 2014	33.5%	1.03 [0.83, 1.29	9]	1		
Lens 2004	13.9%	1.17 [0.83, 1.66	6]	-	-	
MacKie 1991	8.7%	1.14 [0.73, 1.77	7]	-	-	
McManamny 1989	1.7%	1.73 [0.64, 4.64	Į.	_	-	
Miller 2010	0.2%	19.61 [0.95, 403.62	2]			
Moller 2013	11.9%	2.06 [1.42, 3.0	1]		-	
O'Meara 2005	7.4%	0.69 [0.43, 1.12	2]	-	+	
Reintgen 1985	4.9%	1.40 [0.78, 2.52	2]	-	-	
Silipo 2006	0.2%	1.56 [0.11, 21.45	5]		-	
Slingluff 1990	4.8%	1.35 [0.75, 2.44	ļ]	-	-	
Travers 1995	3.8%	1.31 [0.68, 2.59	5]	_	-	
Wong 1989	5.2%	1.14 [0.65, 2.02	2]	_	-	
Zhou 2014	1.5%	0.77 [0.27, 2.20	0]			
Total (95% CI)	100.0%	1.17 [1.03, 1.33	3]		<b>*</b>	
Total events						
Heterogeneity: Chi <sup>2</sup> = 21.05, df = 13 (P = 0.07); $I^2$ = 38%				+	<del>                                     </del>	+
Test for overall effect:	-	, ,,	0.002	0.1	1 10	500
(				avors PAMM	Favors M	M

Overall survival. Patients with pregnancy-associated melanoma (PAM) versus female patients with malignant melanoma (MM). Cl, confidence interval.

prognosi peggiore both overall e disease free survival