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ORIGINAL ARTICLE

Oncological management of pregnancy-associated cancers: analysis from the French CALG (Cancer Associé à La Grossesse) network

Anne-Sophie Boudy[a,b], François Zaccarini[a,b], Lise Selleret[a,b], Alexandra Arfi[a,b], Ilaria Guiggi[a,b], Cyril Touboul[a,b,c], Sofiane Bendifallah[a,b,c] and Emile Darai[a,b,c]

[a]Department of Gynaecology and Obstetrics, Tenon University Hospital, Assistance Publique des Hôpitaux de Paris (AP-HP), University Pierre-et-Marie-Curie Paris VI, Institut Universitaire de Cancérologie (IUC), Paris, France; [b]Centre CALG (Cancer Associé à La Grossesse), Paris, France; [c]UMRS-938 4, Faculté de Médecine Sorbonne Université, Paris, France

ABSTRACT

Background: Pregnancy-associated cancers constitute a major medical challenge. The objective of this study was to describe their epidemiological, oncological and obstetrical outcomes from the French CALG (Cancer Associé à La Grossesse) network.

Material and methods: Retrospective analysis of patients diagnosed with a cancer associated with pregnancy between January 2015 and December 2018 after advice from the CALG network.

Results: Of 218 patients, 197 (90%) were diagnosed with a cancer during pregnancy and 21 the year following delivery. Requests to the CALG network increased from 36 cases in 2015 to 77 cases in 2018. The disease was diagnosed at local and regional stages in 77% of cases. Breast cancer was the most frequent (56%), followed by ovarian (12%) and uterine cervical cancers (10%). Of the 218 patients, 157 (72%) underwent a treatment during pregnancy. Surgery and chemotherapy during pregnancy were performed in 83 patients (83/218, 38%) and 101 patients (46%) at a median term of 17 (IQR 11–24) and 25 (IQR 18–30) WG, respectively. Eighteen (8.5%) of the women had a pregnancy termination, two (1%) an abortion, one (0.5%) a miscarriage, one (0.5%) had a stillbirth and one (0.5%) patient died during pregnancy. The remaining 174 patients (88%) were allowed to continue the pregnancy. Eight recurrences and four deaths were observed with a median follow-up time of 2.6 years (IQR 2.2–3.8).

Conclusions: Our data further describe the incidence and management of pregnancy-associated cancers in western Europe allowing comparisons with other regions.

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Background

Pregnancy-associated cancers are commonly defined as a cancer diagnosed during pregnancy or during the year following delivery. Their prevalence is estimated to be one in 1000–1500 pregnancies [1–3]. Breast, ovarian and uterine cervical cancers are the most frequent with an incidence estimated at 1/1000–1500 for breast cancer and 12–15 per 100,000 pregnancies for uterine cervical cancer [1,4,5]. They constitute a major medical challenge related to the impact on both maternal and fetal outcomes [6,7]. In view of the clinical complexity, a national network – the CALG (Cancer Associé à La Grossesse) network – was created in France in 2008 to help physicians and patients make informed decisions and to obtain epidemiological data for future guidelines [4].

In 2010, an international collaborative study of 215 patients emphasized the obstetrical and neonatal outcomes related to pregnancy-associated cancers, underlining that they should be treated in a multidisciplinary setting with access to maternal and neonatal intensive care units [8]. A 20-year international cohort study of 1170 patients, diagnosed with cancer during pregnancy from 16 countries has recently been published showing that the main pregnancy-associated cancers were breast cancer (39%), uterine cervical cancer (13%), lymphoma (10%), ovarian cancer (7%), leukemia (6%), gastrointestinal cancer (4%) and others (17%) [9]. Follow-up data, including maternal prognosis, were not reported [9].

The objective of this study was to describe national cases of pregnancy-associated cancers and their oncological and obstetrical managements from the CALG network over a short study period thus limiting the risk of biases linked to changes in the FIGO classification and therapeutic approaches.

Material and methods

Study design and participants

This study was a descriptive cohort study involving data from pregnant patients with cancer registered by the CALG

CONTACT Anne-Sophie Boudy annesophie.boudy@aphp.fr Department of Gynaecology and Obstetrics, Tenon University Hospital, Assistance Publique des Hôpitaux de Paris (AP-HP), University Pierre-et-Marie-Curie Paris VI, Institut Universitaire de Cancérologie (IUC), Paris, France; Centre CALG (Cancer Associé à La Grossesse), Paris, France

French Network (Tenon Hospital, Paris, France). The CALG network was established in 2008 to investigate oncological and obstetrical care, and maternal and neonatal outcomes in women with a cancer associated with pregnancy. The present study is a retrospective analysis from the prospective database of the CALG network. The Ethics Committee (CEROG) of the Collège National des Gynécologues et Obstétriciens Français (CNGOF) approved the study (CEROG 2019-GYN-603).

Procedures

Patients diagnosed between January 2015 and December 2018 and for whom advice from the CALG network was requested, were eligible for participation. Patients for whom advice was requested for other reasons – advice about pregnancy consent after cancer, gestational trophoblastic diseases, non-pregnancy-associated cancers – were excluded. Patients with preinvasive disease such as *in situ* adenocarcinoma of the uterine cervix and those with relapses were also excluded (Figure 1).

Diagnosis was systematically proven by histology. For all the patients, epidemiological data (age and parity at diagnosis, genetic mutation, familial of personal history of cancer, term at diagnosis, disease stage), type of cancer and histological features were recorded. Details on oncological, obstetrical and neonatal data were collected.

The disease stage was described for all solid cancers with TNM or FIGO classification. Systemic disease was defined as TNM or FIGO stage IV disease and leukemia; non-systemic disease was defined as TNM or FIGO stages I–III and all brain cancers. Treatment modalities were also recorded.

Statistical analysis

Statistical analyses of the data were performed using R statistical software (Bell Laboratories, Lucent Technologies, Paris, France). Descriptive statistics are shown as medians and IQRs (interquartile range: 25th–75th). The Kaplan–Meier method was used to estimate the cumulative rates (CRs), and comparisons of CRs were made using the log-rank test.

Results

Epidemiological characteristics of the study population

From January 2015 to December 2018, advice from the CALG network was requested for 338 patients. Among them, 120 patients were excluded (61 requests for advice about pregnancy consent after cancer, eight gestational trophoblastic diseases, 17 cancer relapses, 19 carcinomas *in situ* (11 breast carcinomas *in situ* and eight uterine cervical carcinomas *in situ*), 15 non-pregnancy-associated-cancers). Finally, our population was composed of 218 patients; 197 (90%) with a cancer diagnosed during pregnancy and 21 (10%) with a cancer diagnosed during the year following delivery (Figure 1).

Baseline characteristics of the patients are shown in Table 1. Requests to the CALG network increased over the years from 36 cases in 2015 to 77 cases in 2018. Most cancers were diagnosed during the first or second trimester of pregnancy (37% and 39%, respectively).

Characteristics and treatment of pregnancy-associated cancers

Most of the pregnancy-associated cancers were solid tumors (95%). The cancer was diagnosed at local and regional stages in 77% of cases.

Distribution of cancer types and of disease stage is shown in Figure 2. Breast cancer was the most frequent (56%), followed by ovarian cancer (12%) and uterine cervical cancer (10%). Disease stage differed according to the cancer type (Figure 2): ovarian and uterine cervical cancer was mainly diagnosed at early stages while breast cancers were diagnosed at locally advanced stages, and lung cancers at stage IV.

An overview of the various treatment modalities by cancer type is presented in Tables 2 and 3. Positron emission tomography (PET) scans were performed in 23 patients during pregnancy at a median term of 23 weeks of gestation (WG) (IQR 15–30) (Table 3).

Of the 218 patients, 157 (73%) underwent a treatment during pregnancy. Fifty-one patients (32%) had a single treatment modality and 106 (68%) a combination of treatment modalities. Among the 51 patients treated by a single treatment modality, 31 (20%) underwent surgery and 20 (13%) chemotherapy. Combination regimens consisting of more than one chemotherapy agent were recorded for almost all the patients.

Surgery during pregnancy was performed in 83 patients (83/218, 38%) at a median term of 17 (IQR 11–24) WG. Twenty-four patients (24/83, 29%) underwent abdominal surgery during pregnancy including 19 laparoscopies and five laparotomies at a median term of 17 (IQR 15.5–22) and 18 (IQR 14.5–20) WG, respectively. Six patients underwent concomitant abdominal surgery with cesarean section (five for ovarian carcinomas and one for uterine cervical cancer).

Forty-three patients with breast cancer (43/123, 35%) underwent surgery during pregnancy. The median term at diagnosis was 18 WG (IQR 10.5–28.5). For the subpopulation undergoing a surgery, the median term at surgery was 15 (IQR 11–25) WG. Among them, surgery consisted of a partial mastectomy with axillary lymphadenectomy in 10 cases, a partial mastectomy with sentinel node biopsy in 15 cases, a total mastectomy with axillary lymphadenectomy in 10 cases, a total mastectomy with sentinel node biopsy in four cases and a total mastectomy without lymph node evaluation in one case. One patient underwent a sentinel node biopsy without breast surgery before chemotherapy. Two patients underwent a mastectomy with immediate reconstructive surgery (Table 3).

Fourteen patients with ovarian cancer (14/28, 50%) underwent surgery during pregnancy. The median term at diagnosis and at surgery was 14 (IQR 9–19) and 17 (IQR 13.5–19.5)

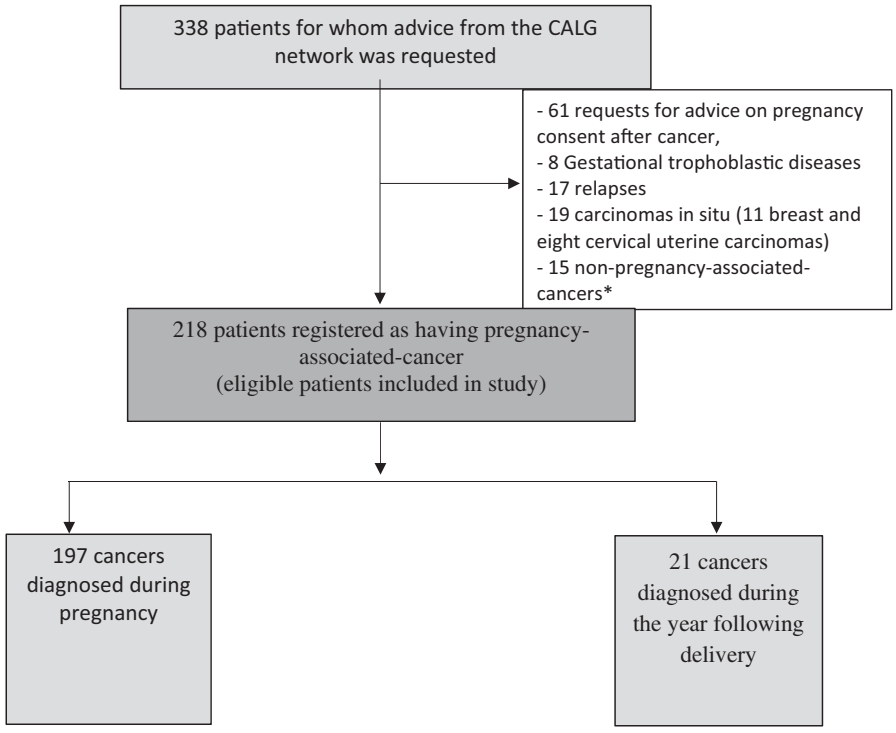

Figure 1. Study scheme. *Non-pregnancy-associated-cancer ($n = 15$): diagnosis of pregnancy during cancer treatment or medically assisted reproduction.

Table 1. Patient characteristics.

	Patients registered as having a cancer associated with pregnancy ($n = 218$)
Age at diagnosis	
Median age (IQR)	34 (31–37)
Missing data	0
Period of diagnosis (%)	
2015	36 (17)
2016	42 (19)
2017	63 (29)
2018	77 (35)
Trimester of diagnosis (%)	
First trimester	81 (37)
Second trimester	84 (39)
Third trimester	32 (15)
Missing data	21 (10)
Parity at diagnosis (%)	
Nulliparous	54 (25)
Multiparous	134 (61)
Missing data	30 (14)
Genetic mutation identified (%)	5 (2)
Stage of disease (%)	
Local or regional	168 (77)
Systemic[a]	29 (13)
Missing data	21 (10)
Medical interruption of pregnancy[b] (%)	18 (8.5)

Data are median (IQR; range) or *n* (%).
[a]Systemic disease was defined as TNM or FIGO stage IV disease and leukemia; non-systemic disease was defined as TNM or FIGO stage I–III and all brain cancers.
[b]Among 197 cancers diagnosed during pregnancy.

WG, respectively. Laparoscopy was performed in 11 cases and laparotomy in three. Surgery consisted of unilateral cystectomy in five cases and unilateral salpingo-oophorectomy in nine. One patient underwent both unilateral cystectomy at 16 WG for unilateral invasive mucinous adenocarcinoma and then unilateral salpingo-oophorectomy with omentectomy, appendectomy and peritoneal biopsies at 20 WG. One patient underwent diagnostic laparoscopy with peritoneal biopsies at 22 WG for a high-grade serous adenocarcinoma of tubo-ovarian origin with peritoneal carcinomatosis. Five patients underwent concomitant cesarean section and surgery for ovarian carcinoma between 36 and 39 WG (three unilateral salpingo-oophorectomies, one unilateral cystectomy and for the last patient peritoneal biopsies for carcinomatosis). No patient underwent lymph node staging during pregnancy (Table 3).

Nine patients with uterine cervical cancer (9/22, 41%) underwent surgery during pregnancy. The median term at diagnosis and at surgery was 17 (IQR 13–27) and 18 (IQR 14–21) WG, respectively. Laparoscopy was performed in five cases for pelvic lymphadenectomy. Among them, one had a second operation 2 weeks later for retroperitoneal para-aortic lymphadenectomy at 14.5 WG. Conization was performed in five cases. Two patients underwent both conization and laparoscopy for pelvic lymphadenectomy. One patient underwent a cesarean section followed by concomitant hysterectomy for per-partum hemorrhage (Table 3).

Chemotherapy was delivered in 101 patients (46%) during pregnancy and initiated at a median term of 25 (IQR 18–30) WG: alkylating agents excluding platinum (62%), anthracyclines (61%), taxanes (37%), antimetabolites (13%) and platinum (14%). Targeted therapy during pregnancy was used for one patient with lymphoma at 30 WG (rituximab). Another patient with chronic myeloid leukemia received Pegasys and hydrea at 14 WG.

Seventy-eight patients with breast cancer (78/123, 63%) started polychemotherapy during pregnancy; alkylating agents excluding platinum with anthracyclines for 45 patients, antimetabolites for four patients, and taxanes for 18 patients at a median term of 26 (IQR 16–30) WG.

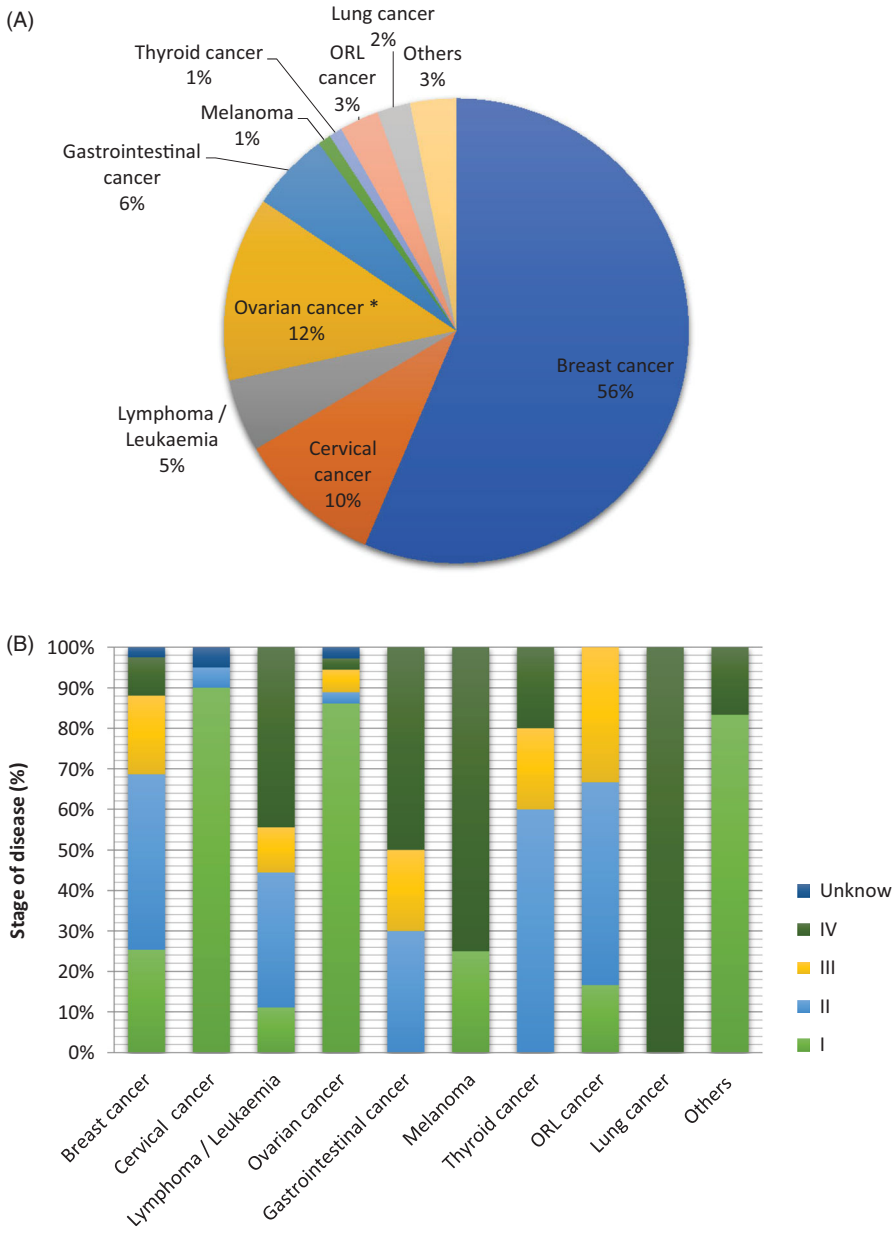

Figure 2. Distribution of cancers during pregnancy (A) and stage of disease at diagnosis by cancer type (B). Disease stage was available for all solid cancers with TNM or FIGO classification. *Ovarian cancers include borderline ovarian tumors. Other: one vaginal cancer/one vulvar cancer/one adenoma carcinoma with unknown primitive tumor/one uterine sarcoma/one peripheral nerve sarcoma/one Ewing sarcoma/one cerebral glioblastoma.

Table 2. Overview of different treatment modalities by cancer type ($n = 218$).

	Total	No treatment (%)	Any surgery (%)	Chemotherapy (%)	Radiotherapy (%)	Targeted/hormonal therapy (%)	Other therapy (%)
Breast	123	0	120 (98%)	101 (82%)	49 (40%)	22 (18%)[a]/47 (38%)[b]	0
Cervical uterine	22	0	18 (82%)	14 (64%)	6 (27%)	0/0	0
Ovarian	28	0	25 (89%)	6 (21%)	0	0/0	0
Leukemia	6	1 (10%)	0	5 (83%)	0	0/0	1 (17%)
Lymphoma	5	0	0	4 (80%)	0	1 (20%)/0	0
Gastro-intestinal	12	0	7 (58%)	10 (83%)	0	1 (8%)/0	1 (8%)
Melanoma	2	0	1 (50%)	1 (50%)	0	0/0	0
Thyroid	2	0	2 (100%)	0	0	0/0	2 (100%) (IRA therapy)
Lung	5	0	0	5 (100%)	1 (20%)	0/0	0
ORL	6		3 (50%)	4 (67%)	3 (50%)	0/0	0
Other	7	0	3 (43%)	4 (57%)	3 (43%)	0/0	0
Total	218	1 (0.5%)	179 (82%)	154 (71%)	62 (28%)	24 (11%)/47 (22%)	4 (2%)

Gastro-intestinal: seven colorectal cancers/two appendix cancers/two stomach cancers/one peritoneal cancer. ORL: three tongue cancers/one parotid cancer/one mandibular cancer/one cavum cancer. Other: one vaginal cancer/one vulvar cancer/one adenoma carcinoma with unknown primitive tumor/one uterine sarcoma/one peripheral nerve sarcoma/one Ewing sarcoma/one cerebral glioblastoma.

[a]Trastuzumab administrated in the postpartum period.

[b]Hormonal therapy administrated in the postpartum period.

Table 3. Different treatment modalities by cancer type and modalities of treatments received and CT PET performed during pregnancy ($n = 218$).

	Total *n* (%)	No treatment during pregnancy (%)	Surgery (%)	Surgery: median term (IQR)	Chemotherapy (%)	Chemotherapy: median term (IQR)	CT PET during pregnancy (%)
Breast	123	24 (20%)	43 (35%)	15 (11–25)	78 (63%)	26 (16–30)	15 (12%)
Cervical uterine	22	9 (41%)	9 (41%)	18 (14–21)	8 (36%)	22 (20–25)	5 (23%)
Ovarian	28	12 (43%)	14 (50%)	17 (13.5–19.5)	2 (7%)	24 (range 22–26)	0
Leukemia	6	5 (83%)	0	NA	0	NA	0
Lymphoma	5	1 (20%)	0	NA	4 (80%)	27 (20–30)	1
Gastro-intestinal	12	4 (33%)	4 (33%)	18 (16.5–25.5)	6 (50%)	25 (19–26)	0
ORL	6	1 (17%)	2 (33%)	23 (range 20–26)	3 (50%)	25 (19–29)	1
Lung	5	3 (60%)	0	NA	0	NA	1
Thyroid	2	0	2 (100%)	13 (range 8–18)	0	NA	0

Median term (gestation weeks).

Two patients with ovarian cancer (2/28, 7%) started chemotherapy based on platinum during pregnancy at a median term of 24 (range 22–26) WG.

Eight patients with uterine cervical cancer (8/22, 36%) started chemotherapy based on platinum and taxanes during pregnancy at a median term of 22 (IQR 20–25) WG.

Survival

Forty-eight patients (37 breast cancers, four uterine cervical cancers, four ovarian cancers, one appendix cancer, one lung cancer, one peripheral nerve sarcoma) had follow-up data available with a median follow-up time of 2.6 years (IQR 2.2–3.8).

During the period study, eight recurrences and four deaths were observed.

The median follow-up for breast cancer was 2.5 years (IQR 2.1–3.8). Six patients experienced a recurrence (6/47, 13%) and three died from the disease (at 3 months, 13.7 months and 31.5 months from diagnosis). One 33-year-old patient had an appendix cancer recurrence 1.5 years after diagnosis. Another 22-year-old patient died during pregnancy 2 weeks after a peripheral nerve sarcoma was diagnosed at 20 WG.

Outcomes of pregnancies

Among the 197 women with cancers diagnosed during pregnancy, 18 (8.5%) had a pregnancy termination, two (1%) an abortion, one (0.5%) a miscarriage, one (0.5%) had a stillbirth and one (0.5%) patient died during pregnancy.

The indications for pregnancy termination were uterine cervical cancer FIGO 1B1 diagnosed at 15 and 16 WG for two patients, locoregional gastrointestinal cancer diagnosed at 23 WG for one, leukemia diagnosed at 7, 14 and 24 WG for three; ovarian cancer diagnosed at 15 WG for one, systemic melanoma at 13 WG for one, systemic lung cancer diagnosed at 15 and 20 WG for two, a Ewing sarcoma diagnosed at 12 WG for one, vaginal cancer diagnosed at 27 WG for one, and breast cancer diagnosed between 4 and 11 WG for six. The remaining 174 patients (88%) were allowed to continue the pregnancy. Ten (55%) of the 18 pregnancy terminations were performed during the first trimester, and eight (45%) during the second. The main reasons for pregnancy termination were requirement of oncological treatment and poor maternal prognosis.

The stillbirth occurred at 32 WG in a 34-year-old patient diagnosed with a borderline ovarian tumor at 15 WG who underwent laparoscopy at 17 WG.

Data about the final outcome of the 174 ongoing pregnancies were available for 92 patients with a live birth. One patient experienced a late miscarriage at 16 WG. Two patients experienced a preterm delivery at 27 and 28 WG. Eight patients (9%) delivered between 32 and 34 WG. Twenty-two patients (24%) delivered between 34 and 37 WG. Forty-four patients (48%) delivered after 37 WG. Other data concerning pregnancy outcomes were missing.

Discussion

The present study is one of the first European studies of a relatively large series of pregnancy-associated cancers over a short period. We report changes in the epidemiology of these cancers with a relatively good prognosis for both patients and newborns.

The strength of our study lies in the analysis of the epidemiology of pregnancy-associated cancers over a period of less than 4 years in a French population hence limiting the risk of bias associated with changes in FIGO classification, therapeutic options and pregnancy management. It is, however, likely that fewer requests for advice were received by the CALG network for cancers diagnosed during the postpartum period as recommended therapeutic strategies are similar to those for non-pregnant women [10–12]. The advice provided by the CALG network doubled over the study period which highlights the fact that physicians are in need of multidisciplinary analysis to manage their patients, and the impact of internet as patients can ask the CALG network for advice directly. As in previous studies, among our 218 patients with a cancer diagnosed during pregnancy, breast cancer represented 56% of the population followed by ovarian (12%), uterine cervical (10%) and digestive cancers (6%) [3,9]. In an Italian study over the period 2001–2012, the risk of pregnancy-related cancer was 122.9 per 100,000 pregnancies but without differentiating between cancers diagnosed during pregnancy from those in the postpartum period. The most common cancers were breast cancer (39.9/100,000 pregnancies), thyroid cancer (15.5/100,000) and lymphomas (13.1/100,000) [3]. The risk of developing a cancer associated with pregnancy increased significantly with age, from 60 of 100,000 for women under 30 years to 265 of 100,000 for women aged over 40 years [3]. In the current study, the

median age of the population was 34 years. Swedish and Australian studies have reported that melanoma is the most frequent cancer diagnosed during pregnancy. This is explained by the characteristics of the Australian population presenting the highest incidence of melanoma in the world [2,6,13,14]. Similarly, in Sweden, melanoma is the third most common cancer in women [15]. Although an increased incidence of melanoma has been observed in France, its incidence is of 4% with 15,404 new cases in 2017 (7343 women), representing the sixth cause of cancer in female but with a median age at diagnosis of 64 years old [16,17]. These considerations underline the variations in the incidence of cancer associated with pregnancy related to the country, the specificities of the populations and probably to the health care systems.

In the current study, ovarian and uterine cervical cancers were the second and third pregnancy-associated cancers pregnancy showing a shift in incidence compared to previous studies [3,5]. Indeed, an international cohort study of de Haan et al., involving 16 countries over a 20-year period, reported that breast cancer was the most frequent cancer associated with pregnancy (39%) followed by uterine cervical cancer (13%), lymphoma (10%) and ovarian cancer (7%) [9]. This apparent discrepancy can be explained by various parameters such as a screening program for uterine cervical cancer and the advent of HPV vaccination, although in France only 27% of the female population are vaccinated. In contrast, de Haan et al.'s study included several countries with various socio-economic levels, no screening program for uterine cervical cancer in some countries and variability in accessing ultrasonography during pregnancy especially during the first trimester [9]. This explains why, in the current study, breast cancer was often diagnosed at locally advanced stages and during the second and third trimesters of the pregnancy while ovarian and uterine cervical cancers were often detected at early stages and during the first trimester French guidelines about the management of pregnancy in the general population impose a Pap smear at the first pregnancy visit for all patients without a Pap smear results under 3 years, and an ultrasonographic exam between 11 and 13 WG [18–20].

A crucial issue is to evaluate the changes in therapeutic strategies. Most (72%) of our patients received treatment during pregnancy as in de Haan et al.'s study where 67% of patients were treated during pregnancy [9]. Regarding treatment modalities, 46% of our patients underwent chemotherapy and 38% surgery. More of our patients had chemotherapy than in de Haan et al.'s study but a similar rate of patients underwent surgery (37% of chemotherapy and 39% of surgery). This suggests that expectant management during pregnancy is decreasing [9]. In our study, only 58 patients (27%) underwent expectant management for cancers diagnosed mainly in the second half of the third trimester allowing a quick delivery or when the disease was compatible with delayed treatment. Anthracycline, alkylan and taxane were the main drugs used during pregnancy as it has been shown that babies exposed *in utero* to these chemotherapies during second and third trimester have good outcomes when a term delivery is achieved [9,21,22]. A meta-analysis by Song et al. including 39 studies published between 1997 and 2018 demonstrated that neoadjuvant platinum-based chemotherapy was a good option to manage uterine cervical cancer during the second and third trimesters [23]. In the same way, several studies have shown the good prognosis of children exposed to anthracyclines during pregnancy [24–26] although this regimen raises concerns about fetal cardiac toxicity [27]. Similarly, taxanes can also be used after the first trimester of pregnancy [28]. Zagouri et al. observed that 90% of the 50 children exposed to taxanes during pregnancy were healthy at 16 months [29]. Conversely, endocrine and targeted therapies should be avoided during pregnancy due to potential adverse neonatal effects [9,22]. When analyzing data according to the main pregnancy-associated cancers, it is important to note variations in treatment. For breast cancer, the rate of chemotherapy and surgery during pregnancy was 63% and 35%, respectively. For ovarian cancer, surgery was mainly proposed as the disease was diagnosed at early stages and terms allowing laparoscopy. Moreover, the incidence of borderline ovarian tumors was 25% ($n = 7/28$) that can be accurately treated by exclusive surgery during pregnancy [30]. Finally, for uterine cervical cancer, the incidence of surgery was also high (41%) linked to diagnosis at early stages.

Another crucial issue is the management of pregnancy. In the current study, 18 pregnancy terminations (8.5%) were performed in accordance with previous studies reporting an incidence of 9–14% emphasizing the high incidence of sparing pregnancies [8,9]. In contrast, Parazzini et al. reported 30% of abortions without distinguishing pregnancy termination from miscarriage [3]. In our experience, it is important to note that while 48% of the patients delivered at term we observed an induced prematurity rate of 42% (32/76), slightly lower than that previously published (48%) [9]. These data have to be analyzed in the light of previous studies. Among 88 patients with uterine cervical cancer treated by platinum-based chemotherapy, Song et al. noted that only 71 of the 88 babies (80.7%) were completely healthy neonates [23]. Moreover, a possible relation between exposure to platinum-taxane-based chemotherapy with low gestational age weight (GAP), and between taxane and admission to neonatal intensive care units have been underlined [9]. Finally, Lu et al. emphasized a higher risk of premature delivery, low GAP and an increase in neonatal mortality mainly related to prematurity [31].

Some limits of the present study deserve to be discussed. First, the retrospective analysis cannot exclude all biases even if the items were extracted from a prospective database. Second, although the study population is relatively low, it represents the largest series in a homogeneous population over a short study period. However, in France, it is important to note that the declaration of pregnancy-associated cancers is not mandatory which implies a potential bias for a comprehensive epidemiological analysis. Moreover, it is possible that only complex cases are addressed to CALG network with a potential bias on the true frequency of various stages of cancer-associated with pregnancy. This is also

probably the case for melanoma as this cancer is often diagnosed at early stage requiring only excision. Third, the inclusion of various pregnancy-associated cancers is a source of difficult interpretation as each cancer has specificities in term of population, modalities of diagnosis and treatments. This explains why we focused on the main pregnancy-associated cancers (breast, ovarian and uterine cervical cancers) representing more than three-quarters of our population and allowing a comparison with previous studies analyzing only one type of cancer. Finally, some data concerning pregnancy outcomes are missing. Moreover, the patient follow-up rate was low despite iterative solicitations by the CALG network of practitioners who have requested an advice. This is important as, after advice from the CALG network, physicians are not obliged to give feed-back about response to therapies, side effects or pregnancy outcomes. In this particular setting, the French health care system should require that oncologists, surgeons and obstetricians systematically provide data about their patients hence contributing to improved knowledge of diseases associated with pregnancy as well as the development of new guidelines.

In conclusion, despite some limits of the present study, our data help better understand the incidence and management of pregnancy-associated cancers in western Europe thus allowing comparisons with other regions.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Smith LH, Danielsen B, Allen ME, et al. Cancer associated with obstetric delivery: results of linkage with the California Cancer Registry. Am J Obstet Gynecol. 2003;189(4):1128–1135.

[2] Lee YY, Roberts CL, Dobbins T, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study. BJOG. 2012;119(13):1572–1582.

[3] Parazzini F, Franchi M, Tavani A, et al. Frequency of pregnancy related cancer: a population based linkage study in Lombardy, Italy. Int J Gynecol Cancer. 2017;27(3):613–619.

[4] Boudy A-S, Naoura I, Selleret L, et al. Propensity score to evaluate prognosis in pregnancy-associated breast cancer: analysis from a French Cancer Network. Breast. 2018;40:10–15.

[5] Eibye S, Kjaer SK, Mellemkjaer L. Incidence of pregnancy-associated cancer in Denmark, 1977–2006. Obstet Gynecol. 2013;122(3):608–617.

[6] Andersson T-L, Johansson ALV, Hsieh C-C, et al. Increasing incidence of pregnancy-associated breast cancer in Sweden. Obstet Gynecol. 2009;114(3):568–572.

[7] Matthews TJ, Hamilton BE. First births to older women continue to rise. NCHS Data Brief. 2014. p. 1–8.

[8] Van Calsteren K, Heyns L, De Smet F, et al. Cancer during pregnancy: an analysis of 215 patients emphasizing the obstetrical and the neonatal outcomes. J Clin Oncol. 2010;28(4):683–689.

[9] de Haan J, Verheecke M, Van Calsteren K, et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. Lancet Oncol. 2018;19(3):337–346.

[10] Loibl S, Schmidt A, Gentilini O, et al. Breast cancer diagnosed during pregnancy: adapting recent advances in breast cancer care for pregnant patients. JAMA Oncol. 2015;1(8):1145–1153.

[11] Amant F, Deckers S, Van Calsteren K, et al. Breast cancer in pregnancy: recommendations of an International Consensus Meeting. Eur J Cancer. 2010;46(18):3158–3168.

[12] De Garnier J, Boudy AS, Selleret L, et al. Expert centre Cancer du sein et Grossesse (CALG): concordance between the proposed therapeutics and those finally received. Gynecol Obstet Fertil Senol. 2019;47(1):36–43.

[13] Andersson T-L, Johansson ALV, Fredriksson I, et al. Cancer during pregnancy and the postpartum period: a population-based study. Cancer. 2015;121(12):2072–2077.

[14] Bray F, Ferlay J, Soerjomataram I, et al. Global Cancer Statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.

[15] Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018;103:356–387.

[16] Institut National du Cancer I. Les cancers en France – Edition 2017 [Internet]; 2018. Available from: https://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Les-cancers-en-France-Edition-2017

[17] Institut National du Cancer I. Les cancers en France. L'essentiel des faits et chiffres/edition 2019 [Internet]; 2019. Available from: https://www.e-cancer.fr/Actualites-et-evenements/Actualites/L-Institut-publie-L-essentiel-des-faits-et-chiffres-des-cancers-en-France-edition-2019

[18] Haute Autorité de Santé H. Dépistage et prévention du cancer du col de l'utérus en France [Internet]; 2013. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2013-08/referentiel-eps_format2clic_kc_col_uterus_2013-30-08__vf_mel.pdf

[19] Haute Autorité de Santé H. Suivi et orientation des femmes enceintes en fonction des situations à risque identifiées [Internet]; 2016. Available from: https://www.has-sante.fr/upload/docs/application/pdf/suivi_orientation_femmes_enceintes_synthese.pdf

[20] Haute Autorité de Santé H. Evaluation de la recherche des papillomavirus humains (HPV) en dépistage primaire des lésions précancéreuses et cancéreuses du col de l'utérus et place du double immuno-marquage p16/Ki67 [Internet]; 2019. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2019-07/synthese_hpv.pdf

[21] Amant F, Vandenbroucke T, Verheecke M, et al. Pediatric outcome after maternal cancer diagnosed during pregnancy. N Engl J Med. 2015;373(19):1824–1834.

[22] Lambertini M, Peccatori FA, Azim HA. Targeted agents for cancer treatment during pregnancy. Cancer Treat Rev. 2015;41(4):301–309.

[23] Song Y, Liu Y, Lin M, et al. Efficacy of neoadjuvant platinum-based chemotherapy during the second and third trimester of pregnancy in women with cervical cancer: an updated systematic review and meta-analysis. Drug Des Devel Ther. 2019;13:79–102.

[24] Avilés A, Neri N, Nambo MJ. Long-term evaluation of cardiac function in children who received anthracyclines during pregnancy. Ann Oncol. 2006;17(2):286–288.

[25] Boudy A-S, Naoura I, Zilberman S, et al. Clues to differentiate pregnancy-associated breast cancer from those diagnosed in postpartum period: a monocentric experience of pregnancy-associated cancer network (CALG). Bull Cancer. 2017;104(6):574–584.

[26] Murthy RK, Theriault RL, Barnett CM, et al. Outcomes of children exposed in utero to chemotherapy for breast cancer. Breast Cancer Res. 2014;16(6):500.

[27] Framarino-Dei-Malatesta M, Sammartino P, Napoli A. Does anthracycline-based chemotherapy in pregnant women with cancer offer safe cardiac and neurodevelopmental outcomes for the developing fetus? BMC Cancer. 2017;17(1):17.

[28] Zheng X, Zhu Y, Zhao Y, et al. Taxanes in combination with platinum derivatives for the treatment of ovarian cancer during pregnancy: a literature review. Int J Clin Pharmacol Ther. 2017;55(9):753–760.

[29] Zagouri F, Sergentanis TN, Chrysikos D, et al. Taxanes for breast cancer during pregnancy: a systematic review. Clin Breast Cancer. 2013;13(1):16–23.

[30] Thomassin-Naggara I, Fedida B, Sadowski E, et al. Complex US adnexal masses during pregnancy: is pelvic MR imaging accurate for characterization? Eur J Radiol. 2017;93:200–208.

[31] Lu D, Ludvigsson JF, Smedby KE, et al. Maternal cancer during pregnancy and risks of stillbirth and infant mortality. J Clin Oncol. 2017;35(14):1522–1529.