

# Practical consensus recommendations for gestational breast cancer

J. S. Sekhon, N. Naik<sup>1</sup>, P. Bansal<sup>2</sup>, I. Bansal<sup>3</sup>, A. Dhull<sup>4</sup>, A. Goel<sup>5</sup>, C. S. Ramachandran<sup>6</sup>, S. Shinde<sup>7</sup>, S. Aggarwal<sup>8</sup>, P. M. Parikh<sup>9</sup>

## Abstract

This manuscript provides a practical and easy to use consensus recommendation to community oncologists on how to manage gestational breast cancer.

**Key words:** Anthracycline, blue dye, breast conservative surgery, fetal monitoring, inducing delivery, taxane, trimesters

## Introduction

Gestational breast cancer (or pregnancy-associated breast cancer) is defined as breast cancer that is diagnosed during pregnancy, in the first postpartum year, or any time during lactation.<sup>[1]</sup> The incidence of pregnancy associated breast cancer is approximately 15 to 35 per 100,000 deliveries.<sup>[2,3]</sup> Most pregnancy-associated breast cancers are seen in women under the age of 30, amounting to almost 20% of the population.<sup>[4,5]</sup> The diagnosis and management of gestational breast cancer is generally similar to that in nonpregnant patients, with a few changes to account for the maternal and foetal well being. The outcomes of women with gestational breast cancer have been found to be conflicting. One study showed no difference in progression free and overall survival.<sup>[6]</sup> Another study showed better disease free survival, and OS.<sup>[7]</sup> A meta-analysis carried out in 2012, found a higher risk of death in pregnancy – associated breast cancer, mostly in women diagnosed in the postpartum period.<sup>[8]</sup> A retrospective analysis of 26 women from a tertiary care centre in India with a median follow up of 33 months showed a median progression free period of 18 months, and 3 year survival of 50%.<sup>[9]</sup> All patients had infiltrating duct carcinoma. The median age of the patients was 26 years, 73% of the patients were diagnosed postpartum. Most of the patients had locally advanced disease at presentation, and 30.7% of the patients had distant metastases at presentation.

The expert group met to discuss and arrive at a consensus statement to provide community oncologists practical guidelines on the management of gestational breast cancer. This manuscript is the outcome of the expert group discussion and consensus arrived at in May 2017.

## Defining Clinical Cohort and Practice of Expert Group Panel Members

The primary objective was to provide a consensus statement for community oncologists that could be applicable as ready-to-use practical recommendations. Hence, the applicable setting was outlined by defining the clinical cohort and current practice of the participating delegates and expert group panel members – on the basis of which this document was prepared.

The expert group discussed a hypothetical clinical scenario of a 26 year old lady, primigravida, who was seven months pregnant when diagnosed with nonmetastatic operable, infiltrating duct carcinoma, ER/PR/Her2 neu positive. A series of questions on key practical issues and management challenges were asked, with each question answerable in the form of selection from multiple choice options. The consensus answers were used as the basis of formulating the consensus statement providing community oncologists with ready-to-use practical recommendations. The national and international experts invited to this meeting were also provided the data on the voting by the audience delegates. Members of the panel were also allowed to share their personal experiences, make comments and record dissent while voting for the consensus statements.

## Diagnosis and Staging

The panel recommended that breast ultrasound is the imaging test of choice while evaluating breast lumps in pregnant patients. Mammography may be carried out only with appropriate abdominal shielding; however sensitivity may be low in view of increased breast density, increased water content and loss of contrasting fat.<sup>[10-13]</sup> The experts recommended that breast magnetic resonance imaging (MRI) without contrast may be considered if ultrasound and mammogram are noncontributory.<sup>[14]</sup> Core biopsy is safe and feasible in pregnant patients, and must be carried out in order to confirm diagnosis.<sup>[15,16]</sup>

The experts agreed that chest X-ray with abdominal shielding and abdominal ultrasound should be used for staging patients with clinically locally advanced breast cancer. CT scan is not recommended because of concerns of foetal radiation exposure. MRI without contrast may be used, however should be avoided during the first trimester.<sup>[14]</sup>

## Treatment – Surgery

The experts recommended that surgical resection is the mainstay of treatment in pregnant patients with breast cancer, and is safe in all 3 trimesters of pregnancy.<sup>[3,17-21]</sup> The attending oncologists also agreed with the same, as reflected by the poll results. The panel did not recommend inducing premature delivery in case of patients with operable breast cancer. 57% of the oncologists polled agreed with waiting till foetal maturity was achieved [Tables 1 and 2]. The panel also agreed that breast conservation surgery (BCS) is a suitable option for patients with operable breast cancers who are in their 2<sup>nd</sup> or 3<sup>rd</sup> trimester of surgery. Breast conservation

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Department of Medical Oncology, Fortis Hospital, Ludhiana, Punjab, <sup>1</sup>Department of Surgical Oncology, Dharamshila Cancer Hospital, <sup>2</sup>Department of Surgical Oncology, Max Hospital, Departments of <sup>3</sup>Surgery and <sup>4</sup>Medical Oncology, Sir Ganga Ram Hospital, <sup>5</sup>Department of Medical Oncology, NCR, New Delhi, <sup>6</sup>Department of Medical Oncology, Asian Institute of Medical Sciences, Faridabad, <sup>7</sup>Department of Radiation Oncology, Artemis Hospital, Gurugram, <sup>8</sup>Department of Radiation Oncology, PGIMS, Rohtak, Haryana, <sup>9</sup>Department of Oncology, Shalby Cancer and Research Institute, Mumbai, Maharashtra, India

**Correspondence to:** Dr. J. S. Sekhon,  
E-mail: jagdev.sekhon@ymail.com

surgery in suitable patients may be considered after proper counselling and discussion with the patient.<sup>[22-24]</sup> This was reflected by the poll results as 83.3% of the oncologists polled agreed with the panel [Tables 3 and 4]. Mastectomy is preferred during the first trimester, in view of concerns regarding delaying radiotherapy. At present, axillary nodal dissection is the standard of care in pregnant patients. The role of sentinel lymph node biopsy (SLNB) is still uncertain.<sup>[25-28]</sup> One study enrolled 26 pre-menopausal, non-pregnant women who underwent peritumoral injection of ~12 MBq of <sup>99m</sup>Tc-HSA nanocolloids. The study showed no radiotracer concentration except in the injection site and in the sentinel node, and concluded that LS and SLNB can be performed safely during pregnancy.<sup>[28]</sup> The experts examined the evidence and decided that presently there is insufficient safety data with regard to lymphoscintigraphy (LS). The panel recommends if SLNB is performed, blue dye should be avoided, as it is associated with the risk of an anaphylactic maternal reaction.<sup>[29]</sup> The opinion was divided amongst the polled oncologists, as seen in Tables 5-7. The panel also recommended that immediate reconstruction/oncoplastic surgery should be avoided. Reconstruction preferably should be better carried out postpartum, and should be restricted to a prosthetic implant.<sup>[30]</sup>

### Treatment – Chemotherapy, Targeted Therapy and Hormone Therapy

The experts were of the opinion that chemotherapy may be given during 2<sup>nd</sup> and 3<sup>rd</sup> trimesters safely, once the period of organogenesis is over.<sup>[3,31-33]</sup> Anthracyclines can be safely used.<sup>[34-38]</sup> After examining the current evidence, the panel recommended that taxanes may also be given.<sup>[39]</sup> Methotrexate is not recommended during the entire period of pregnancy.<sup>[34,40]</sup> Frequent foetal monitoring and ultrasound is important, fetal lung maturity must be carefully determined before delivery. Chemotherapy should be stopped at 33 weeks of pregnancy, so that the delivery and/or, surgery can be safely carried out, giving sufficient time for recovery from chemotherapy induced platelet and neutrophil nadir. Breast feeding is contraindicated during chemotherapy, targeted therapy and hormone therapy. The placenta should also be sent for histo-pathological examination to rule out occult metastases.

The panel does not recommend radiation therapy during pregnancy. Radiation therapy may be given after delivery. The panel agrees with international guidelines that second pregnancy may be feasible two years after completing therapy.<sup>[3]</sup>

### Take Home Message

- The panel does not recommend inducing premature delivery in case of patients with operable breast cancer
- Surgery is safe in all 3 trimesters of pregnancy and is the treatment of choice in patients being treated with curative intent
- Breast conservation surgery is a suitable option for patients with operable breast cancers who are in their 2<sup>nd</sup> or 3<sup>rd</sup> trimester of surgery
- Presently there is insufficient safety data with regard to both LS and SLNB and hence it is not recommended as standard of care. Sentinel node biopsy may be done during pregnancy, however blue die should not be used
- Immediate reconstruction/oncoplastic surgery should be avoided

**Table 1: Question categories addressed by the expert panel**

| Broad question title                           | Number of sub questions |
|--|-------------------------|
| Optimum treatment of gestational breast cancer | 1                       |
| Timing of various treatment options            | 1                       |
| Role of surgery in gestational breast cancer   | 3                       |
| Role of chemotherapy/targeted therapy          | 1                       |

**Table 2: Question 1 - In a 7 month pregnant patient with newly diagnosed nonmetastatic breast cancer, is inducing premature delivery recommended before definitive therapy**

| Options                          | Yes  | No   |
|----------------------------------|------|------|
| Percentage of polled oncologists | 42.9 | 57.1 |

Expert group consensus: Inducing premature delivery not recommended

**Table 3: Question 2 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, what is the optimum treatment option?**

| Options                          | Surgery | NACT |
|----------------------------------|---------|------|
| Percentage of polled oncologists | 75      | 25   |

Expert group consensus: Optimal treatment for such a patient is surgery for breast cancer with curative intent. NACT=Neoadjuvant chemotherapy

**Table 4: Question 3 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, is breast conservation surgery a suitable option?**

| Options                          | Yes  | No   |
|----------------------------------|------|------|
| Percentage of polled oncologists | 83.3 | 16.7 |

Expert group consensus: BCS is a suitable option in pregnant patients provided if feasible - nonpregnancy related contraindications still apply. BCS=Breast conservation surgery

**Table 5: Question 4 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer who refuses surgery, is trastuzumab based chemotherapy an option?**

| Options                          | Trastuzumab based chemotherapy | No trastuzumab chemotherapy |
|----------------------------------|--------------------------------|-----------------------------|
| Percentage of polled oncologists | 20                             | 80                          |

Expert group consensus: Targeted therapy with trastuzumab is contraindicated in pregnant patients

**Table 6: Question 5 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer is lymphoscintigraphy and sentinel lymph node biopsy safe?**

| Options                          | Yes  | No   |
|----------------------------------|------|------|
| Percentage of polled oncologists | 66.7 | 33.3 |

Expert group consensus: LS and/or SLNB are not recommended as standard of care in pregnant patients since there is insufficient safety data. LS=Lymphoscintigraphy, SLNB=Sentinel lymph node biopsy

**Table 7: Question 6 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, can one go for primary surgery followed by oncoplastic surgery?**

| Options                          | Yes | No |
|----------------------------------|-----|----|
| Percentage of polled oncologists | 70  | 30 |

Expert group consensus: Immediate reconstruction/oncoplastic surgery should be avoided

- Chemotherapy may be given during 2<sup>nd</sup> and 3<sup>rd</sup> trimesters safely. Anthracyclines are safe, and taxanes may also be given. Methotrexate is not recommended

- Chemotherapy should be stopped at 33 weeks of pregnancy
- Frequent fetal monitoring and ultrasound is important, fetal lung maturity must be carefully determined
- Breast feeding is to be avoided while receiving systemic cancer directed therapy
- Trastuzumab is not recommended in pregnant patients
- Placenta should be sent for histopathologic examination to rule out metastasis
- Second pregnancy may be feasible two years after completing therapy
- The panel does not recommend radiation therapy during pregnancy. Radiation therapy may be given after delivery.

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### Conflicts of interest

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