Best Doctors®

Name:

Date of Birth:

Best Doctors Report Summary

This Best Doctors' Report Summary highlights and clarifies the key points of your Expert report(s). You can use this as an aid when you read the report(s) and in the future when you review and discuss the report(s) with your treating physician(s). We are always available to you and your treating team should there be any additional questions or concerns.

[redacted] recommends that you and your treating physician(s) review and consider the following assessment and options:

- [redacted] agrees with the pathology re-review that suggests that you have breast cancer.
- [redacted] recommends that you see a surgeon. [redacted] thinks that you require excision of the superior lesion to completely remove the tumor with negative margins. Surgical options include lumpectomy versus mastectomy.
- [redacted] recommends obtaining a left axillary ultrasound. If you have a suspicious left axillary lymph node, [redacted] recommends considering a fine needle aspirate. In patients with positive axillary lymph nodes, chemotherapy prior to surgery (neoadjuvant chemotherapy) is sometimes recommended.
- If you opt for lumpectomy you will require post-operative radiation therapy. Even if you undergo mastectomy you may require radiation if you have multiple positive axillary lymph nodes.
- [redacted] thinks that your tumor needs to be tested for ER/PR and HER2. If your tumor is ER+/PR+ you will require adjuvant hormonal therapy. If your tumor is HER2+ you may be a candidate for trastuzumab combined with chemotherapy.
- [redacted] recommends genetic testing for BRCA mutations. If you have a BRCA mutation you should undergo bilateral salpingo-oophorectomies and consider prophylactic bilateral mastectomies.

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BEST DOCTORS EXPERT REPORT

Best Doctors®

[redacted]

Dear Ms. [redacted]

Please find enclosed the Best Doctors' InterConsultation™ final report.

This comprehensive report is the result of a three step process: medical information gathering, analysis of the information and a Specialist's thorough review. It includes an assessment of your condition, the answers to the specific questions you have asked as well as the biographic details of Best Doctors' network Specialist selected to review your case. We have also added information that explains the way Best Doctors works to your treating doctors.

The objective of the InterConsultation report is not to provide a medical diagnosis or therapeutic recommendations on their own, but to complete the information that you have received from your own doctors about your medical condition and treatment options thus helping you to have a better understanding of them.

If following an in-depth reading of the InterConsultation report additional questions arise, we will be very pleased to answer and clarify them for you. We strongly recommend that you discuss this report with your treating doctors.

In the meantime, we thank you for allowing Best Doctors to assist you with your medical needs. Please do not hesitate to contact us in the future if we can be of any further assistance.

Sincerely,

Dr. Malaxechevarría

Medical Team

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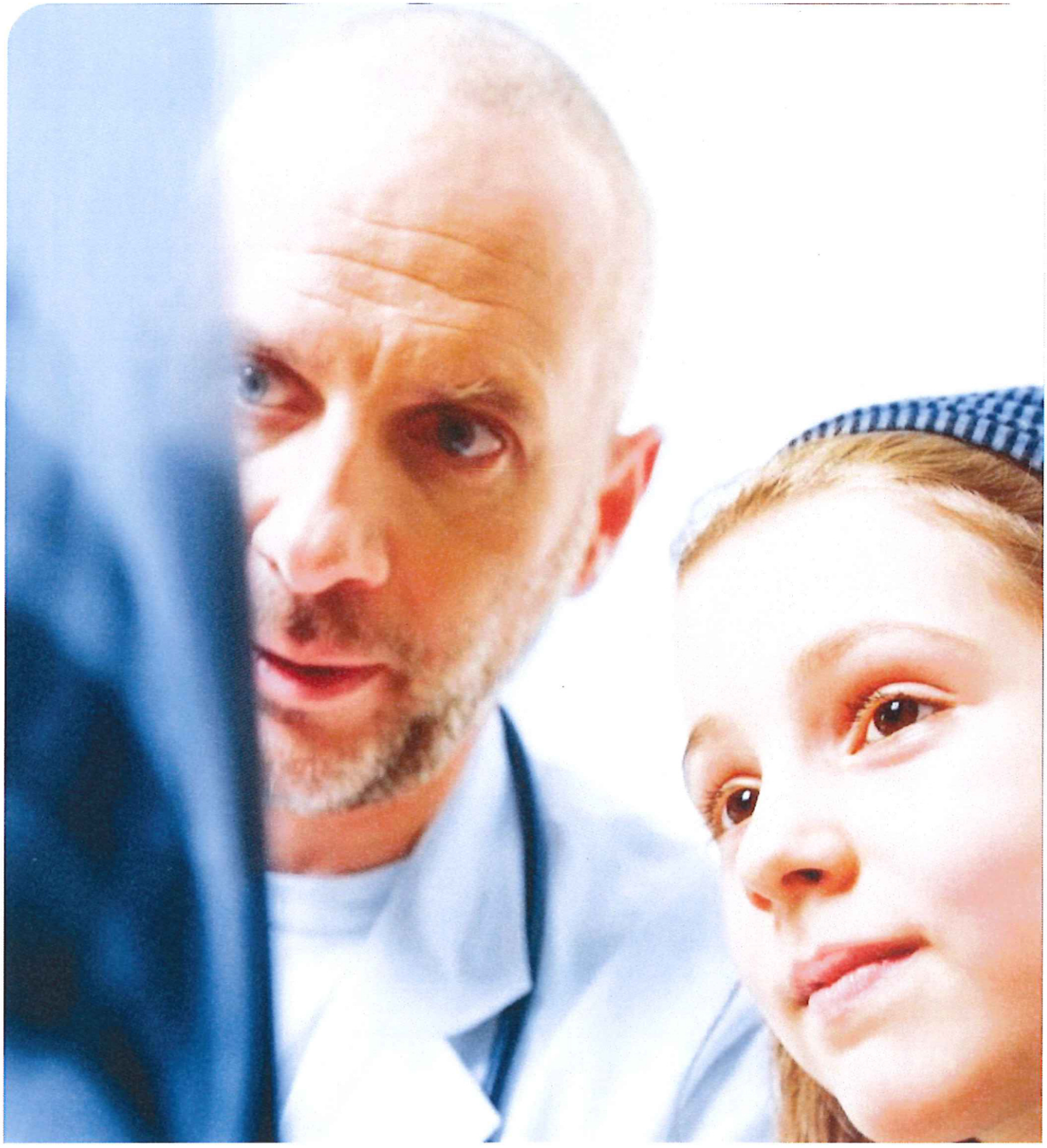


YOUR EXPERT
RESPONSE

[redacted]

Dr. [redacted]
Medical Director
Best Doctors, Inc.

Re: [redacted]
DOB: [redacted]

Dear Dr. [redacted]

I am pleased to provide an InterConsultation for the above referenced individual at the request of Best Doctors®. As you have stated, the purpose of this is to provide a second opinion and to discuss treatment options.

To summarize the background medical history, [redacted] is a 50-55 year-old woman who presents with a recent diagnosis of left breast cancer. On [redacted] routine screening mammography demonstrated an area of architectural distortion as well as a separate area of indeterminate microcalcifications in the left breast. No abnormalities were noted on left breast ultrasound. Physical examination demonstrated a left axillary nodule which the patient had noted chronically but was recently enlarged by her report. Stereotactic biopsies of the two breast lesions performed on [redacted] were interpreted as negative for malignancy as per a report from an outside hospital. The patient remained concerned because of intermittent left breast pain and flattening of the left nipple. Pathology review from UHN pathologists as part of her Best Doctors review demonstrated focal invasive ductal carcinoma measuring 0.4 cm in maximum dimension in the superior-most mammographic abnormality. The predicted histologic grade was I/III (low grade).

[redacted] past medical history is notable for a diagnosis of chronic IgA nephropathy for which she underwent a living related donor renal transplant in July of 1999. She is on chronic immunosuppressive therapy. She also is treated for hypertension and hyperlipidemia. Her family history is notable for a sister who died of complications

resulting from ovarian cancer. I am asked to comment on her evaluation to date and the treatment plan.

In response to the specific questions that have been asked:

1. **What is your overall assessment of the patient's condition? What is the differential diagnosis for this patient? What do you think is the most likely diagnosis and why?**
   Distinguishing invasive ductal carcinoma from benign breast tissue can be challenging in core needle biopsies based on the small amount of tissue that is available for review. This is particularly true for low grade tumors, which more closely resemble normal breast tissue than high grade malignancies. The differential diagnosis in this case therefore includes invasive ductal carcinoma, as per the UHN pathology review, versus benign fibrocystic breast tissue. Three UHN breast pathologists have reviewed the slides and they all concur that the diagnosis is in fact invasive ductal carcinoma. I therefore strongly favor this diagnosis.

2. **The UHN pathology review has significantly revised the previous diagnosis; can you comment on the clinical implications of the change of diagnosis for this patient?**
   The diagnosis of invasive ductal carcinoma significantly changes the treatment recommendations. Benign breast disease (such as fibrocystic disease) does not require any additional treatment. Invasive ductal carcinoma, in contrast, requires additional therapy. The first important step is to see a surgeon. Now that the diagnosis of invasive cancer has been established, the patient requires surgical excision of the area surrounding the stereotactic biopsy site to completely remove the malignancy with adequate margins. Further treatment (e.g. radiation therapy, chemotherapy and hormonal therapy) will be based on the results of the pathology as detailed in question #5 below.

3. **What is your interpretation of the imaging studies reviewed?**
   There were two areas of concern on the mammogram. In the superior aspect of the breast there was an area of architectural distortion. This mammographic finding is very concerning for malignancy, as it suggests that there is an underlying mass retracting the surrounding breast tissue. The biopsy which demonstrated malignancy was obtained from this region. The second mammographic abnormality demonstrated calcifications. Calcifications are fairly common on mammograms and have a variety of different morphologies (e.g. coarse vs. fine, clustered vs. scattered); some appearnces are highly suspicious for cancer, while others appear benign. The calcifications in the case of [redacted] were "indeterminate" – they did not have characteristic features of either malignancy or benign changes. The biopsy showed no evidence of malignancy or atypia; this interpretation is consistent at both the original institution and the UHN pathology department. I would conclude, therefore, that

[redacted] has only one focus of cancer in the superior aspect of her left breast and the area containing calcifications represents benign breast tissue.

4. **What additional diagnostic testing do you recommend (please include information regarding additional imaging, serum tumor marker testing, ER/PR and Her2Neu testing and potential genetic testing given the patient's family history of a first degree relative with ovarian cancer)?**
To design an optimal treatment plan it will be important to know the estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu status of the invasive cancer. Given the small sample size of the biopsy, these tests may be best performed on the repeat excision that will be required as part of her surgical management. It may be possible to perform at least the ER/PR staining on the current specimen.

   The enlarged left axillary lymph node needs to be addressed. I would recommend a left axillary ultrasound. If the lymph node appears abnormal, I would consider a fine needle aspirate to determine whether it is positive for carcinoma.

   I would hold off on any further staging until the patient has undergone additional surgical evaluation. Serum tumor markers are of little value in a patient with early stage breast cancer and I don't routinely send them in my patients. Their only real value is to monitor the progress of patients with known metastatic disease. [redacted] has already had a chest X-ray which was normal. If she has high risk pathology (e.g. positive lymph nodes) I would consider a bone scan and abdominal imaging (e.g. an abdominal ultrasound) to complete her staging evaluation.

   I would recommend genetic testing for BRCA1/2 mutations. Given [redacted] own history of breast cancer and the history of ovarian cancer in her sister there is increased risk of a genetic predisposition to breast and ovarian cancer. If [redacted] were known to carry a deleterious BRCA mutation I would strongly recommend bilateral salpingo-oophorectomy (removal of the ovaries and fallopian tubes). She would also be a candidate for prophylactic mastectomies.

5. **What treatment options exist? What are the relative advantages and disadvantages of each option? How would you recommend proceeding in this case?**
The treatment of breast cancer can be broken down into *local* and *systemic* treatment. *Local* treatment is used to remove the tumor from the breast and minimize the risk of recurrence within the breast or chest wall. This involves surgery, with or without radiation therapy. Surgical options include lumpectomy versus mastectomy. From a long-term survival viewpoint these two options are considered to be equivalent. Lumpectomy requires post-surgical radiation treatment to lower the risk of local relapse (within the breast), but has obvious cosmetic advantages. Mastectomy greatly reduces the risk of local relapse since

very little breast tissue remains, and oftentimes radiation therapy is not necessary. In selected patients (e.g. patients with multiple involved lymph nodes) radiation may be recommended even if they have undergone mastectomy.

Systemic treatment is administered to lower the risk of relapse at distant metastatic sites. Options include chemotherapy and hormonal therapy. Hormonal therapy is typically recommended for patients with ER+/PR+ disease, which underscores the importance of performing these tests. Chemotherapy is typically recommended for patients with high risk disease. High risk features would include large tumor size, positive lymph nodes, ER-/PR- or HER2+ disease. HER-2/neu is an oncogene that is over-expressed in 15-20% of patients with breast cancer. In these patients the cancer behaves in a more aggressive fashion. Trastuzmab (Herceptin) is a monoclonal antibody therapy that targets the HER2 protein and is typically combined with chemotherapy in patients with HER2+ breast cancer.

6. **How would you recommend following this patient?**
Breast cancer surveillance is very simple after active therapy is completed. I typically see my patients every 3 - 6 months for physical examination and review of systems. I would not typically recommend any routine testing other than annual mammography. There is no evidence that obtaining further routine radiographic testing (e.g. CT scans, PET scans, bone scans) or laboratory testing in an asymptomatic patient is of benefit. The key to surveillance is to appropriately evaluate any new symptoms. For example, should [redacted] develop a new symptom such as back pain, more often than not this will be a routine problem such as a muscle strain, but I would have a lower threshold to obtain radiographic studies given her breast cancer history if the pain was unusually intense or prolonged.

7. **What is the patient's prognosis?**
The prognosis will be based on the additional pathology data determined from the definitive surgery. The five most important features that determine prognosis are:
    - Tumor size
    - Number of involved lymph nodes
    - Histologic grade
    - ER/PR status
    - HER2 status

    Once these features are known the information can be entered into an online risk prognostication tool (www.adjuvantonline.com) that will estimate the 10-year risk of relapse. I would comment that the absolute goal of treatment in the case of [redacted] is long-term cure, which is very realistic in most patients with breast cancer.

8. **If not addressed by the questions above, please provide any further recommendations that you believe will aid in understanding this patient's findings or in guiding future therapeutic decisions.**

The salient features of [redacted]'s case have been addressed in the questions outlined above.

9. **How does member's status as a kidney transplant recipient (and the associated chronic immunosuppression) affect her treatment recommendations and prognosis?**
   This would have the greatest impact if she has high risk pathology for which chemotherapy is recommended. Most chemotherapy drugs temporarily lower the white blood count and thus increase the risk of bacterial infections. In a patient on chronic immunosuppressive therapy, the risk of infection would be further increased. If chemotherapy was felt to be of benefit based on her prognostic indicators, her oncologist would clearly need to have a conversation with her nephrologist regarding treatment options. She could probably be treated with a reasonably low risk using white blood cell stimulating shots (e.g. Neulasta or Neupogen) and/or prophylactic antibiotics during her white blood cell nadir.

10. **Please provide scientific references that may be helpful to the treating physicians and the patient, and/or that lend support to your recommendations.**

    [redacted] would benefit from reading Judy Kneece's book "Breast Cancer Treatment Handbook: Understanding the Disease, Treatments, Emotions, and Recovery from Breast Cancer", which is an excellent introduction to breast cancer treatment. I would be happy to provide additional scientific references once her pathology data are available.

In summary, [redacted] is a 50-55 year-old woman who recently presented with a left breast mammographic abnormality. Pathology has been reviewed by UHN pathologists, and the diagnosis of invasive ductal carcinoma has been established. Recommendations include the following:

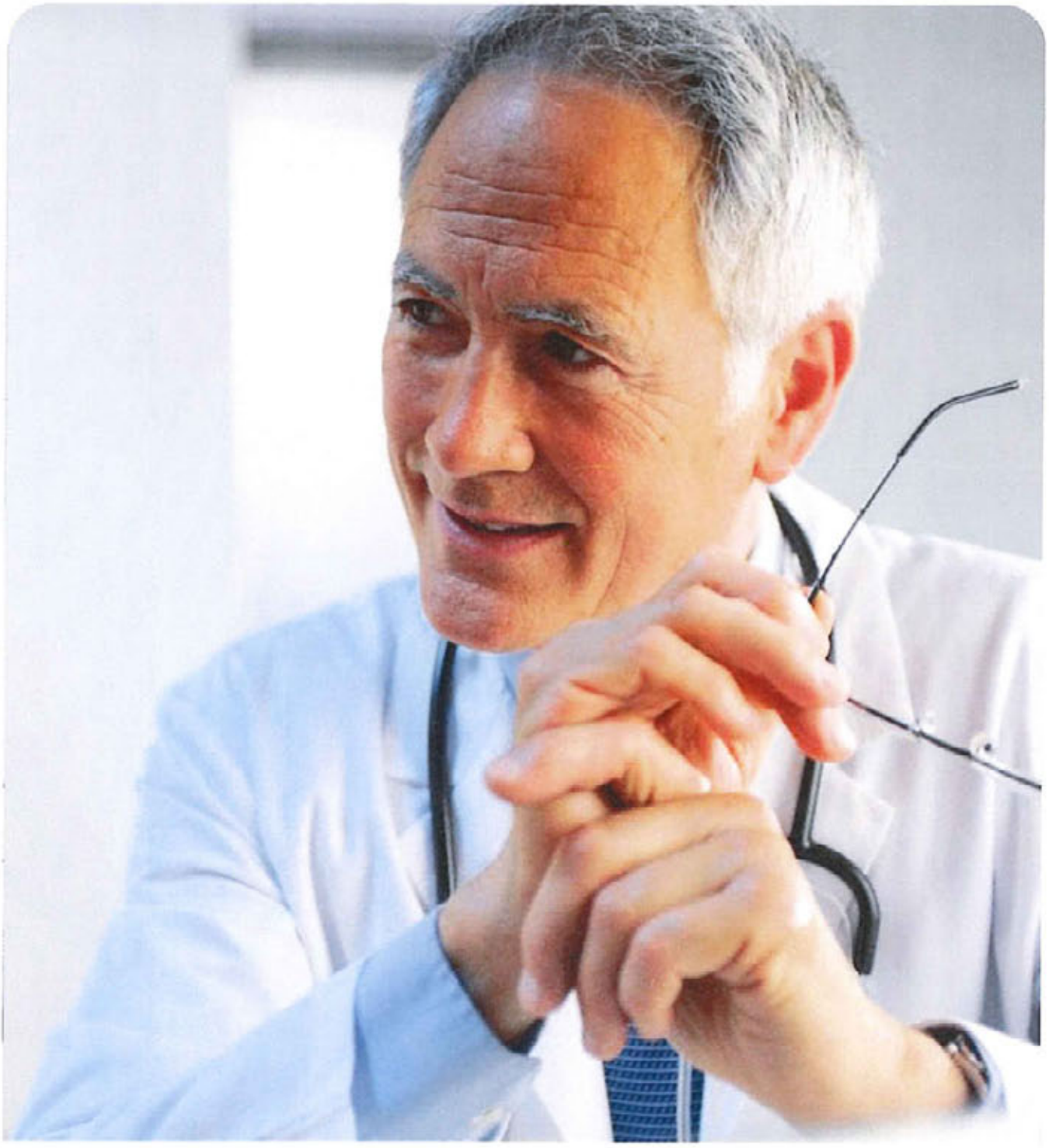
- I would see a surgeon expeditiously. She requires excision of the superior lesion to completely remove the tumor with negative margins. Surgical options include lumpectomy versus mastectomy.
- I would obtain a left axillary ultrasound. If she has a suspicious left axillary lymph node, I would consider a fine needle aspirate. In patients with positive axillary lymph nodes we will sometimes recommend chemotherapy prior to surgery (neoadjuvant chemotherapy).
- If she opts for lumpectomy she will require post-operative radiation therapy. Even if she undergoes mastectomy she may require radiation if she has multiple positive axillary lymph nodes.
- Her tumor needs to be tested for ER/PR and HER2. If the tumor is ER+/PR+ she will require adjuvant hormonal therapy. If the tumor is HER2+ she may be a candidate for trastuzumab combined with chemotherapy.

- I would recommend genetic testing for BRCA mutations. If she has a BRCA mutation she should undergo bilateral salpingo-oophorectomies and consider prophylactic bilateral mastectomies.

I hope that this information is helpful to you, and I wish the patient the very best of luck.

Sincerely yours,

[redacted]



BEST DOCTORS
EXPERT BIOGRAPHY

Consulted Physician

[redacted]

Medical Oncology and Hematology

[redacted] Hospital
[redacted] Center
[redacted]
[redacted]
[redacted]
[redacted]

Profile

Medical School: [redacted]

Residency: [redacted]

Intern: [redacted]

Fellowship: [redacted]

Titles

Medical Director, [redacted], [redacted] Hospital

Summary

Specialty	Sub Specialty
Medical Oncology and Hematology	Breast Cancer
Medical Oncology and Hematology	General Medical Oncology and Hematology

INFORMATION
FOR YOUR TREATING PHYSICIAN

BEST DOCTORS MEDICAL ANALYTICAL PROCESS®

AN IN-DEPTH REVIEW IDENTIFICATION OF KEY MEDICAL ISSUES

INFORMATION GATHERING

The Best Doctors member interacts by phone with a Member Advocate, a Registered Nurse.

The Member Advocate gathers the member's medical records including diagnostic test results and pathology for review.

INFORMATION ANALYSIS

The Best Doctors Clinical Team analyses and reviews all information.

The key medical issues are identified and the most appropriate specialist is chosen from the Best Doctors global network of 50,000.

SOLUTIONS

The Best Doctors expert assesses the case, confirming the diagnosis or offering an alternative. Treatment recommendations are provided.

The member receives a Comprehensive Report which summarises all findings and which the member may choose to share with their treating physician.

Best Doctors service doesn't end with the Comprehensive Report. Our services are available to our members whenever questions and concerns arise.

DOCTORS HELPING DOCTORS

BEST DOCTORS INTERCONSULTATION™

At the heart of our service is the InterConsultation – an extensive and detailed review of a member´s medical files including diagnostic tests and pathology.

A multidisciplinary team of physicians revise the medical records, identify the pertinent issues and formulate the clinical questions – essentially deconstructing and reconstructing the diagnosis.
If the case involves pathology, the specimens are redone at a Center of Excellence using the latest staining techniques.

Once the review is complete, the appropriate specialist(s) from the Best Doctors, global network of 50.000 world-renowned, peer-nominated specialists is selected to assess the clinical synopsis, confirm the diagnosis and recommend treatment plan options.

This report offers the treating physician an opportunity to consult with top medical experts, which is an additional resource that otherwise may not be available to them.
The InterConsultation provides additional knowledge, answers specific questions, reassures regarding the diagnosis and provides treatment plan recommendations.

Without having to leave home or change doctors, the members, together with their treating physician, are enabled to make informed decisions about their care.

HOW ARE BEST DOCTORS EXPERTS CHOSEN?

Simply put, their medical peers recommend them. Only experts currently incorporated into the Best Doctors global network receive our survey to nominate and vote for Best Doctors experts.

Our survey asks one simple question, representing the way that doctors find the best care for themselves and their families:

"If you or a loved one needed a doctor in your specialty, whom would you choose?"

The specialist nominated to the network is then screened for licensure, certification and disciplinary actions. To ensure the integrity of our network, we initiate the process every 18 months.

Over the past 20 years, the Best Doctors global network has grown to 50.000 specialists.
Best Doctors does not provide, nor accept fees for the privilege of inclusion in the network.
Specialists can only be accepted into the network through a peer-reviewed nomination poll. Best Doctors does not publish or sell the names of specialists in our network.