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Onco News

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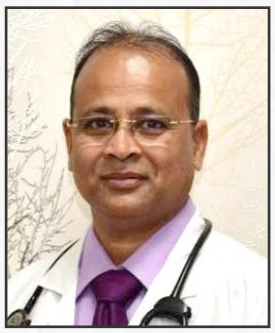
From the Desk of Editor



Dear readers!

Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancers with an estimated 1.67 million new cancer cases . There is a significant increase in the incidence and cancer-associated morbidity and mortality in Indian subcontinent as described in global and Indian studies. Earlier cervical cancer was most common cancer in Indian woman but now the incidence of breast cancer has surpassed cervical cancer and is leading cause of cancer death. Sadly maximum patients in India presents in stage III or IV, leading to dismal outlook. Lot of advances have happened in management of metastatic breast cancer(MBC).We can expect survival of three years or so in most of these patients.

With regards
Dr. Naresh Somani
M.D., D.M.

Metastatic Breast Cancer (MBC)

MBC (also called stage IV) is breast cancer that has spread to another part of the body, most commonly the liver, brain, bones, or lungs. Cancer cells can break away from the original tumor in the breast and travel to other parts of the body through the bloodstream or the lymphatic system, which is a large network of nodes and vessels that works to remove bacteria, viruses, and cellular waste products.

Breast cancer can come back in another part of the body months or years after the original diagnosis and treatment. Nearly 30% of women diagnosed with early-stage breast cancer will develop metastatic disease. Some patients have MBC when they are first diagnosed with breast cancer (called “de novo metastatic”). This means that the cancer in the breast wasn't detected before it spread to another part of the body. A metastatic tumor in a different part of the body is made up of cells from the breast cancer. So if breast cancer spreads to the bone, the metastatic tumor in the bone is made up of breast cancer cells, not bone cells. Many people continue to live long, productive lives with breast cancer in this stage. There are a wide variety of treatment options for MBC, and new medicines are being tested every day.

MBC Symptoms and Diagnosis

The symptoms of MBC can vary greatly depending on the location of the cancer.

MBC Treatment and Planning

The main goals of MBC treatment are the following:

- Longest survival possible with the disease
- Fewest possible side effects from the cancer and its treatment
- Best and longest quality of life possible

There is no cure for metastatic cancer, but a good quality of life is possible for months or even years.

Treatment options for MBC vary based on:

- Site of Metastasis
- The presence and level of hormone receptors and/or HER2 in the tumor.
- Gene mutations in the tumor
- Specific symptoms
- Previous cancer treatments
- Patients overall healh

Contd.

Chemotherapy

Chemotherapy is used in the treatment of MBC to damage or destroy the cancer cells as much as possible. Agents like Capecitabine, Carboplatin, Cisplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Pegylated liposomal doxorubicin, Epirubicin, Eribulin, Fluorouracil, Gemcitabine as single agent or in combination chemotherapy is used for this purpose.

Radiation Therapy

Radiation therapy is the use of high-energy x-rays or other particles to kill cancer cells. Radiation therapy may be used to shrink or slow tumor growth. It can also treat symptoms from the cancer, such as pain.

Hormonal Therapy

Hormonal therapy, also called endocrine therapy, is an effective treatment for many tumors that test positive for either ER or PR.

Hormone receptor-positive tumors may use hormones to fuel their growth. The goal of this type of therapy is to lower the levels of estrogen and progesterone in the body or to block these hormones from getting to cancer cells. Options for hormonal therapy include:

- Tamoxifen: Tamoxifen is a drug that blocks estrogen from binding to breast cancer cells. It is a pill taken daily by mouth. Common side effects of tamoxifen include hot flashes as well as vaginal discharge or bleeding.
- Aromatase Inhibitors : Aromatase inhibitors(Anastrazole;Letrozole or Exemustine) decrease the amount of estrogen made by tissues other than the ovaries in women who have gone through menopause by blocking the aromatase enzyme. This enzyme changes hormones called androgens into estrogen when the ovaries have stopped making estrogen after menopause.
- Ovarian suppression: This is the use of drugs or surgery to stop the ovaries from producing estrogen. It may be used in combination with tamoxifen or an aromatase inhibitor. Drugs called gonadotropin or luteinizing releasing hormone (GnRH or LHRH) analogs can stop the ovaries from making estrogen,

MBC Symptoms and Diagnosis

The symptoms of MBC can vary greatly depending on the location of the cancer. analogs can stop the ovaries from making estrogen, causing temporary menopause. Surgery permanently stops estrogen production. Ovarian suppression is commonly used to treat hormone receptor-positive metastatic breast cancer in pre menopausal women, as complete estrogen suppression may be helpful against the cancer.

- Fulvestrant: Fulvestrant is a selective estrogen receptor downregulatr. It binds to the estrogen receptors, blocking the ability of estrogen to attach to these receptors. Unlike other oral hormonal therapies, fulvestrant is given monthly by an injection into a muscle.
- Combination hormonal therapy: Newer agents like CDK4/6 inhibitors have improved results greatly of single agents like letrozole or fulvistrant.

Targeted Therapy

Targeted therapies target specific characteristics of cancer cells, such as a protein that allows the cancer cells to grow in a rapid or abnormal way. Targeted cancer therapies are treatments that target specific characteristics of cancer cells, such as a protein that allows the cancer cells to grow in a rapid or abnormal way. Targeted therapies are generally less likely than chemotherapy to harm normal, healthy cells. Some targeted therapies are antibodies that work like the antibodies made naturally by our immune systems. These types of targeted therapies are sometimes called immune targeted therapies.

Targeted therapy for metastatic HER2-positive breast cancer

HER2-targeted therapies can be used to treat HER2-positive metastatic breast cancer. Some of these drugs may be used together with chemotherapy. In general, for a person with HER2-positive metastatic breast cancer, there is almost always a HER2-targeted therapy being used along with another systemic therapy.

- **Trastuzumab:** For MBC, trastuzumab can be given in combination with different types of chemotherapy or with hormonal therapy. Trastuzumab can be given as a weekly infusion, or once every 3 weeks. Patients receiving trastuzumab have a small (2% to 5%) risk of heart problems and should have monitoring with an echocardiogram periodically.
- **Pertuzumab:** Research shows that adding pertuzumab to trastuzumab and chemotherapy as part of first-line therapy for HER2-positive metastatic breast cancer lengthens lives with few additional side effects. Based on this data, the combination of trastuzumab, pertuzumab, and chemotherapy has become a standard of care for the first-line treatment of untreated metastatic HER2-positive breast cancer.
- **Ado-trastuzumab emtansine or T-DM1:** This is have previously received trastuzumab and chemotherapy with either paclitaxel or docetaxel.

  T-DM1 is a combination of trastuzumab linked to very small amount of a strong chemotherapy.

Contd.

For the management of metastatic breast cancer patients

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AbNib

Lapatinib Tablets I.P. 250 mg

More life to every moment!

BRAND NAME: AbNib
GENERIC NAME: Lapatinib Tablets IP 250 mg

WARNING: HEPATOTOXICITY
Hepatotoxicity has been observed in clinical trials and post marketing experience. The hepatotoxicity may be severe and deaths have been reported. Causality of the deaths is uncertain.

Abbreviated Prescribing Information
COMPOSITION:

Each Film-Coated Tablet Contains:

Lapatinib Ditosylate IP	
Equivalent to Lapatinib	250mg
Excipients	q.s.
Colours: Red oxide of Iron & Yellow oxide of Iron.	

INDICATION: In combination with capecitabine it is indicated in patients with advanced or metastatic breast cancer whose tumour overexpress HER2 and who have received prior therapy including trastuzumab. In combination with letrozole for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated Lapatinib in combination with trastuzumab, indicated for the treatment of patients with hormone receptor- negative metastatic breast cancer whose tumours overexpress HER2/neu (ErbB2) and who have progressed on prior trastuzumab therapy in combination with chemotherapy in the metastatic setting. **DOSE & METHOD OF ADMINISTRATION:** Lapatinib treatment should only be initiated by a physician experienced in the administration of anti-cancer medicinal products. HER2 (ErbB2) overexpressing tumours are defined by IHC3+, or IHC2+ with gene amplification or gene amplification alone. HER2 status should be determined using accurate and validated methods. **Posology:** *Lapatinib / capecitabine combination posology:* The recommended dose of Lapatinib is 1250 mg (i.e. five tablets) once daily continuously. The recommended dose of capecitabine is 2000 mg/m2/day taken in 2 doses 12 hours apart on days 1-14 in a 21day cycle. Capecitabine should be taken with food or within 30 minutes after food. Please refer to the full prescribing information of capecitabine. *Lapatinib / trastuzumab combination posology.* The recommended dose of Lapatinib is 1000 mg (i.e. four tablets) once daily continuously. The recommended dose of trastuzumab is 4 mg/kg administered as an intravenous (IV) loading dose, followed by 2 mg/kg IV weekly. Please refer to the full prescribing information of trastuzumab. *Lapatinib / aromatase inhibitor combination posology:* The recommended dose of Lapatinib is 1500 mg (i.e. six tablets) once daily continuously. When coadministered with Lapatinib, the recommended dose of letrozole is 2.5 mg once daily. Please refer to the full prescribing information of the co-administered aromatase inhibitor for dosing details. ***Dose delay and dose reduction:*** *Cardiac events:* Lapatinib should be discontinued in patients with symptoms associated with decreased left ventricular ejection fraction (LVEF) that are National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) grade 3 or greater or if their LVEF drops below the institutions lower limit of normal. Lapatinib may be restarted at a reduced dose (750 mg/day when administered with trastuzumab, 1000 mg/day when administered with capecitabine or 1250 mg/day when administered with an aromatase inhibitor) after a minimum of 2 weeks and if the LVEF recovers to normal and the patient is asymptomatic. *Interstitial lung disease / pneumonitis:* Lapatinib should be discontinued in patients who experience pulmonary symptoms which are NCI CTCAE grade 3 or greater. *Diarrhoea:* Lapatinib dosing should be interrupted in patients with diarrhoea which is NCI CTCAE grade 3 or grade 1 or 2 with complicating features (moderate to severe abdominal cramping, nausea or vomiting greater than or equal to NCI CTCAE grade 2, decreased performance status, fever, sepsis, neutropenia, frank bleeding or dehydration). Lapatinib may be reintroduced at a lower dose (reduced from 1000 mg/day to 750 mg/day, from 1250 mg/day to 1000 mg/day or from 1500 mg/day to 1250 mg/day) when diarrhoea resolves to grade 1 or less. Lapatinib dosing should be permanently discontinued in patients with diarrhoea which is NCI CTCAE grade 4. *Other toxicities:* Discontinuation or interruption of dosing with Lapatinib may be considered when a patient develops toxicity greater than or equal to grade 2 on the NCI CTCAE. Dosing can be restarted, when the toxicity improves to grade 1 or less, at 1000 mg/day when administered with trastuzumab, 1250 mg/day when administered with capecitabine or 1500 mg/day when administered with an aromatase inhibitor. If the toxicity recurs, then Lapatinib should be restarted at a lower dose (750 mg/day when administered with trastuzumab, 1000 mg/day when administered with capecitabine or 1250 mg/day when administered with Letrozole). *Renal impairment:* No dose adjustment is necessary in patients with mild to moderate renal impairment. Caution is advised in patients with severe renal impairment as there is no experience of Lapatinib in this population. *Hepatic impairment:* Patients with severe hepatic impairment (Child-Pugh Class C) should have their dose of Lapatinib reduced. A dose reduction from 1250 mg/day to 750 mg/day (HER 2 -positive metastatic breast cancer indication) or from 1500 mg/day to 1000 mg/day (hormone receptor – positive, HER2 positive breast cancer indication) in patients with severe hepatic impairment is predicted to adjust the area under (AUC) to the normal range and should be considered. Lapatinib should be discontinued if changes in liver function are severe and patients should not be retreated. Administration of Lapatinib to patients with moderate to severe hepatic impairment should be undertaken with caution due to increased exposure to the medicinal product. Insufficient data are available in patients with hepatic impairment to provide a dose adjustment recommendation. *Elderly:* There are limited data on the use of Lapatinib / capecitabine and Lapatinib / trastuzumab in patients aged ≥ 65 years. No overall differences in efficacy and safety of the combination of Lapatinib and letrozole were observed between these patients and patients < 65 years of age. *Paediatric population.* The safety and efficacy of Lapatinib in children below the age of 18 years have not yet been established. No data are available. ***Method of administration:*** The daily dose of Lapatinib should not be divided. Lapatinib should be taken either at least one hour before, or at least one hour after food. To minimise variability in the individual patient, administration of Lapatinib should be standardised in relation to food intake, for example always to be taken one hour before a meal. Missed doses should not be replaced and the dosing should resume with the next scheduled daily dose. ***CONTRAINDICATIONS:*** Lapatinib is contraindicated in patients with known severe hypersensitivity (e.g., anaphylaxis) to this product or any of its components. ***WARNINGS & PRECAUTIONS:*** *Cardiac toxicity:* Lapatinib has been associated with reports of decreases in LVEF. Lapatinib has not been evaluated in patients with symptomatic cardiac failure. Caution should be taken if Lapatinib is to be administered to patients with conditions that could impair left ventricular function (including co-administration with potentially cardiotoxic medicinal products). Evaluation of cardiac function, including LVEF determination, should be conducted for all patients prior to initiation of treatment with Lapatinib to ensure that the patient has a baseline LVEF that is within the institutions normal limits. LVEF should continue to be evaluated during treatment with Lapatinib to ensure that LVEF does not decline to an unacceptable level. In some cases, LVEF decrease may be severe and lead to cardiac failure. Caution should be taken if Lapatinib is administered to patients with conditions that could result in prolongation of QTc (including hypokalemia, hypomagnesemia, congenital long QT syndrome), co-administration of other medicinal product known to cause QT prolongation, or conditions that increase the exposure of lapatinib, such as co-administration of strong CYP3A4 inhibitors. Hypokalemia or hypomagnesemia should be corrected prior to treatment. Electrocardiograms with QT measurement should be performed prior to and one to two weeks after the start of Lapatinib therapy. When clinically indicated, e.g. after initiation of a concomitant treatment that might affect QT or that may interact with lapatinib, ECG measurement should also be considered. *Interstitial lung disease and pneumonitis:* Lapatinib has been associated with reports of pulmonary toxicity including interstitial lung disease and pneumonitis. Patients should be monitored for symptoms of pulmonary toxicity (dyspnoea, cough, fever) and treatment discontinued in patients who experience symptoms which are NCI CTCAE grade 3 or greater. Pulmonary toxicity may be severe and lead to respiratory failure. *Hepatotoxicity:* Hepatotoxicity has occurred with Lapatinib use and may in rare cases be fatal. The hepatotoxicity may occur days to several months after initiation of treatment. At the initiation of treatment, patients should be advised of the potential for hepatotoxicity. Liver function (transaminases, bilirubin and alkaline phosphatase) should be monitored before the initiation of treatment and monthly thereafter, or as clinically indicated. Lapatinib dosing should be discontinued if changes in liver function are severe and patients should not be retreated. Patients who carry the HLA alleles DQA1*02:01 and DRB1*07:01 have increased risk of Lapatinib-associated hepatotoxicity. In a large, randomised clinical trial of Lapatinib monotherapy (n=1,194), the cumulative frequency of severe liver injury (ALT >5 times the upper limit of normal, NCI CTCAE grade 3) at 1 year of treatment was 2.8% overall. The cumulative frequency in DQA1*02:01 and DRB1*07:01 allele carriers was 10.3% and in non-carriers was 0.5%. Carriage of the HLA risk alleles is common (15 to 25%) in Caucasian, Asian, African and Hispanic populations but lower (1%) in Japanese populations. Caution is warranted if Lapatinib is prescribed to patients with moderate or severe hepatic impairment. Caution is advised if Lapatinib is prescribed to patients with severe renal impairment. **PREGNANCY AND LACTATION:** Pregnancy category D. There are no adequate well controlled studies in adult pregnant women. **ADVERSE REACTIONS:** The safety of lapatinib has been evaluated as monotherapy or in combination with other chemotherapies for various cancers in more than 20,000 patients, including 198 patients who received lapatinib in combination with capecitabine, 149 patients who received lapatinib in combination with trastuzumab and 654 patients who received lapatinib in combination with letrozole. The most common adverse reactions (>25%) during therapy with lapatinib were gastrointestinal events (such as diarrhoea, nausea, and vomiting) and rash. Palmar-plantar erythrodysesthesia [PPE] was also common (>25%) when lapatinib was administered in combination with capecitabine. The incidence of PPE was similar in the lapatinib plus capecitabine and capecitabine alone treatment arms. Diarrhoea was the most common adverse reaction resulting in discontinuation of treatment when lapatinib was administered in combination with capecitabine, or with letrozole. No additional adverse reactions were reported to be associated with lapatinib in combination with trastuzumab. There was an increased incidence of cardiac toxicity, but these events were comparable in nature and severity to those reported from the lapatinib clinical programme. These data are based on exposure to this combination in 149 patients in the pivotal trial. **ISSUED ON:** SOURCE: Prepared based on full prescribing information, Version 1.0-- dated 23rd December, 2018

For additional information, please contact Medical Services Division
Abbott India Limited, Floor 17, Godrej BKC, Plot No. C – 68, BKC,
Near MCA Club, Bandra (E), Mumbai - 400 051.

Abbott

This allows the drug to deliver chemotherapy into the cancer cell while lessening the chemotherapy received by healthy cells. T-DM1 is given by every 3 weeks.

Lapatinib: Women with HER2-positive metastatic breast cancer may benefit from lapatinib when other medications are no longer effective at controlling the cancer's growth. The combination of lapatinib and the chemotherapy capecitabine is approved to treat metastatic HER2-positive breast cancer when a patient has already received chemotherapy and trastuzumab. The combination of lapatinib and 2positive and ER-positive cancer. Lapatinib is also used in combination with trastuzumab for patients whose cancer is growing while receiving trastuzumab. Lapatinib may be able to enter into the brain, and could be an option for HER2-positive breast cancer that has spread to the brain.

Onco Facts

Updates in Chronic Lymphocytic Leukemia-

- **Ibrutinib/Rituximab Improves OS, PFS Versus FCR for Untreated CLL**

  The combination of ibrutinib and rituximab significantly improved overall survival and progression-free survival compared with standard fludarabine, cyclophosphamide, and rituximab for younger patients with chronic lymphocytic leukemia.
- **Venetoclax/Rituximab Combo Achieves Durable, High MRD-Negative Status in CLL**

  The combination of venetoclax and rituximab for relapsed/refractory chronic lymphocytic leukemia produced high rates of undetectable minimal residual disease, which was associated with prolonged progression-free survival.

Upcoming Activities of SoMex

1. SoMex will organize **"3rd Neuro Critical Care Update 2019"** at the Pink City Jaipur on 29th & 30th June 2019 (Organizing Secretary Dr. Sunit Shah).
2. SoMex will organize **"3rd Precision Oncology and Annual International Breast Cancer conference 2019"** at the Pink City Jaipur from 11-13 October, 2019 (Organizing Secretary Dr. Sandeep Jasuja).

BOOK - POST

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If undelivered please return to:
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