Cancer Education Day
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Shared Care: Breast Cancer Survivorship

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WINDSOR REGIONAL HOSPITAL
OUTSTANDING CARE – NO EXCEPTIONS!

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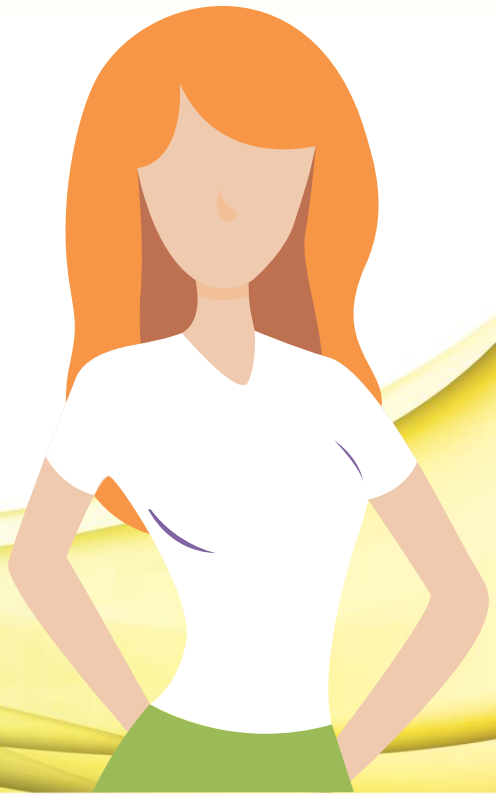
Conflicts of Interest

- None to declare **(Drs. Kadri & Gupta)**

Case 1

- A 50 year old female
- Screening mammogram is positive:
  - Diagnosed with Invasive Ductal Carcinoma
  - Undergoes lumpectomy with sentinel lymph node biopsy, adjuvant chemotherapy and radiation
  - Remains on tamoxifen and has been followed by the wonderful team at the Windsor Regional Cancer Centre.



Case 1

- **Past Med Hx:** Hypothyroidism, Type II DM (diet controlled)
- **Medications**: Synthroid
- **Menarche**: Age 12
- **Menopause**: Age 51
- No pregnancies **G0P0**
- No breastfeeding
- **No smoking**
- **Rare ETOH**
- **Family Hx:** 2 maternal great aunts – breast CA, cousin breast CA, Father Type II DM

Case 1: Survivorship Follow-up

- She is now 2 year post diagnosis and treatment. She is seeing you for an AHE, you are managing her Type II diabetes. She wonders: **“How frequently should I be seen?”**
- **“I have been discharged from the Windsor Regional Cancer Program. Should I be following up with the Windsor Regional Cancer Program?”**

Survivorship

An individual is considered a cancer survivor from the time of diagnosis, during and immediately after treatment, and for the rest of their life.

Survivor care should include the following:

- Surveillance for recurrence and screening for subsequent primary cancer
- Prevention of new or recurrent cancer
- Surveillance for late physical or psychological effects
- Interventions for consequence of cancer treatment and effects (e.g. medical, financial, social or psychological)

Follow-up for Survivors

Survivorship Years	Frequency of Follow-up
1-3 years	Every 6-12 months
4+ years	Every 12 months

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Guidelines for Survivorship Visit

Survivorship Years	Frequency of Follow-up	History	Physical
1-3 years	Every 6-12 months	• Breast lumps • Mastectomy scar changes • Breast axillary and/or supraclavicular masses/lesions • Bone pain • Cough • Abnormal vaginal bleeding (for women taking tamoxifen) • Fatigue • Unexplained weight loss • Anorexia	• Breast exam • Regional Lymph nodes • Chest wall • Lungs and abdomen • Arms for lymphedema
4+ years	Every 12 months		

Survivorship Assessment - Patient Version

Survivorship Concerns	Survivorship Care Survey
Cardiac Toxicity	1. Do you have shortness of breath or chest pain after physical activities (eg, climbing stairs) or exercise? Yes/No 2. Do you have shortness of breath when lying flat, wake up at night needing to get air, or have persistent leg swelling? Yes/No
Anxiety, Depression, Trauma, and Distress	3. In the past two weeks, have you been bothered more than half the days by little interest or pleasure in doing things? Yes/No 4. In the past two weeks, have you been bothered more than half the days by feeling down, depressed, or hopeless? Yes/No 5. Has stress, worry, or being nervous, tense or irritable interfered with your life? Yes/No
Cognitive Function	6. Do you have difficulties with multitasking or paying attention? Yes/No 7. Do you have difficulties with remembering things? Yes/No 8. Does your thinking seem slow? Yes/No
Fatigue	9. Do you feel persistent fatigue despite a good night's sleep? Yes/No 10. Does fatigue interfere with your usual activities? Yes/No 11. How would you rate your fatigue on a scale of 0 (none) to 10 (extreme) over the past week? 0–10
Lymphedema	12. Since your cancer treatment, have you had any swelling, fatigue, heaviness, or fullness on the same side as your treatment that has not gone away? Yes/No
Hormone-Related Symptoms	13. Have you been bothered by hot flashes/night sweats? Yes/No 14. Have you been bothered by other hormone-related symptoms (ex, vaginal dryness, incontinence)? Yes/No
Pain	15. Are you having any pain? Yes/No 16. How would you rate your pain on a scale of 0 (none) to 10 (extreme) over the past month? 0–10
Sexual Function	17. Do you have any concerns regarding your sexual function, sexual activity, sexual relationships, or sex life? Yes/No 18. Are these concerns causing you distress? Yes/No
Sleep Disorder	19. Are you having problems falling asleep, staying asleep, or waking up too early? Yes/No 20. Are you experiencing excessive sleepiness (ie, sleepiness or falling asleep in inappropriate situations or sleeping more during a 24-hour period than in the past)? Yes/No 21. Have you been told that you snore frequently or that you stop breathing during sleep? Yes/No
Healthy Lifestyle	22. Do you engage in regular physical activity or exercise, such as brisk walking, jogging, weight/resistance training, bicycling, swimming, etc.? Yes/No ▸ 22a. If you answered "Yes," how often? 23. Excluding white potatoes, do you eat at least 2½ cups of fruits and/or vegetables each day? Yes/No 24. Do you have concerns about your weight? Yes/No 25. Do you take vitamins or supplements? Yes/No
Immunizations and Infections	26. Have you received your flu vaccine this flu season? Yes/No 27. Are you up to date on your vaccines? Yes/No/Don't know

Surveillance

- If patient has had a bilateral mastectomy, no need to follow with mammography
- If breast reconstruction using tissue from another part of body, consider mammography

Survivorship Years	Mammography
1-3 years	Every 12 months
4+ years	Every 12 months

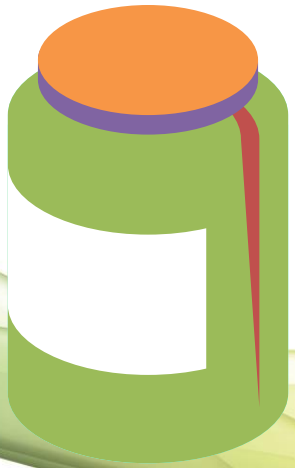
To MRI or not to MRI?

- If thought to be high risk, should be referred to Ontario Breast Screening High Risk Screening Program. If MRI is not medically appropriate, breast ultrasound could be ordered with the mammogram.
- High risk patient aged 30-69:
  - Is known to have gene mutation
  - Has a first degree relative with a gene mutation
  - Has personal or family history of breast or ovarian cancer
  - Has h/o chest radiation before age 30 and longer than 8 years prior

Case 2: Medication Side Effects

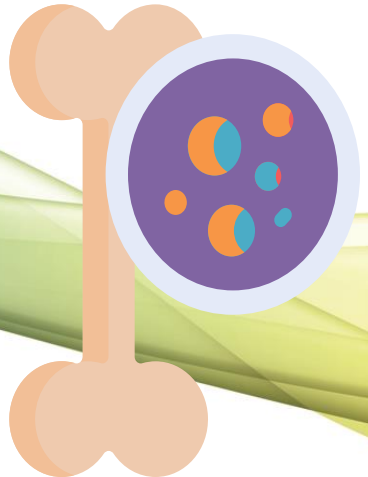
- You are seeing her at a 3 year post diagnosis follow up appointment and she asks:

“I am still taking Tamoxifen are there any other tests that I should have done?”



Bone Mineral Density

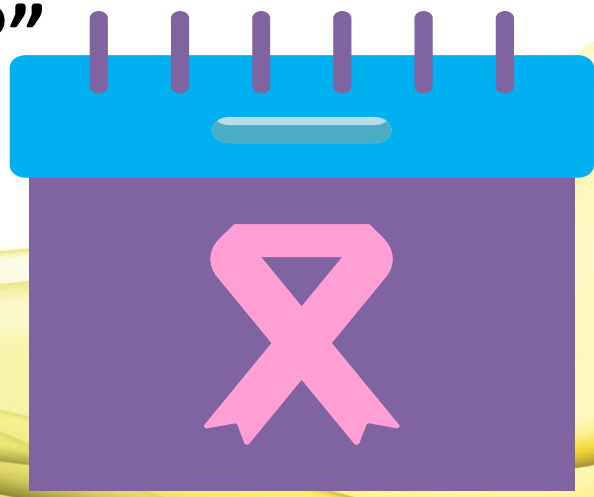
- Yearly lab work with cholesterol profile for patients on aromatase inhibitors.
- DEXA scans every 2 years for:
  - Women taking an aromatase inhibitor
  - Premenopausal women taking tamoxifen/gonadotropin releasing hormone
  - Women with chemotherapy induced premature menopause.



Case 3: Medication Risks

- 6 months later….
- She is back for a follow-up. She has not had a menstrual period for 3 and half years and yesterday she started spotting. She is still taking tamoxifen.

“What should I do, is this normal ?”



Post-Menopausal Bleeding on Tamoxifen

- Stop Tamoxifen
- Refer to gynaecology for pelvic ultrasound and endometrial biopsy

Case 3

- The work-up for post-menopausal bleeding is negative for Endometrial Cancer.
- She was found to have vaginal dryness and irritation.

“Should I continue taking Tamoxifen?”

Case 3

Treatment:

- Vaginal moisturizers, vaginal gels, Replens, Astroglide, topical Vitamin D or E.
- Vaginal lubricants
- Limited data is available in breast cancer survivors with local estrogen treatments with rings and suppositories.
- Other topical hormones
- Referral to Gynaecology for specialized treatments like laser therapy

Case 4: Long Term Effects

- At the same follow-up appointment she asks:

“I am experiencing some swelling in my arms. Is that normal?”

Common Long Term Effects

PHYSICAL	• Surgery related pain, numbness, stiffness • Irradiation-related, erythema, swelling, tenderness, edema • Lymphedema • Menopausal symptoms associated with systemic treatment
PSYCHOSOCIAL	• Depression and anxiety • Cognitive effects • Changes in sexual function and fertility • Challenges with body and self-image • Return to work challenges • Financial challenges

Lymphedema

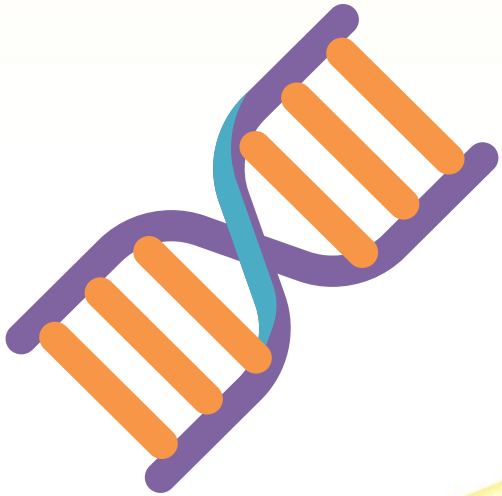
- Surgery, radiation, increased number of lymph nodes removed, higher stage of disease and obesity increases risk.
- Early diagnosis and management is key.
- Management includes self-education.
- Refer to Certified Lymphedema Therapist for compression garments, manual lymph drainage, progressive resistance training under supervision.
- Refer to physical therapy for range of motion exercises.

Case 5:Relapse

- A 56-year old breast cancer survivor is seen in your office. She is now 6 years post breast cancer diagnosis.

Case 5

- **Past Med Hx:** Breast Cancer Stage II treated with bilateral mastectomy with primary reconstruction in 2013
- **Medications**: None. Previously on Tamoxifen discontinued in 2018
- **Menarche**: Age 11
- **Menopause**: Age 50
- No pregnancies **G0P0**
- No breastfeeding
- **No smoking**
- **Rare ETOH**
- **Family Hx:** Mother- Breast Ca, Sister- Breast Ca
- High Risk Breast Screening Program genetic testing: BRCA 1 **gene mutation**



Case 5

- Presenting Complaint: Lower back pain x 8 weeks which has been worsening despite conservative management. No red flags on history
- You order an X-ray of the lumbar spine and pelvis

Case 5

- Results: X-ray shows a ?lytic lesion in the pelvis
- You order a bone scan which confirms a lytic lesion and malignancy in the bone
- You promptly refer her back to the Windsor Regional Cancer Centre

Case 5

- Relapse can happen beyond 5 years time.
- Consideration to be made for extended treatment beyond 5 years for all patients on Tamoxifen and high risk patients on Aromatase inhibitors.
- Consider referral back at 5 year point in those patients if interested in extended treatment.

Case 5

- Our patient was found to be postmenopausal.
- She underwent CT C/A/P which was negative for other sites of disease.
- Bone biopsy confirmed metastatic breast cancer ER/PR positive and HER2 negative.
- Patient started Letrozole and Palbociclib with good response.

Response Rates in a First-Line Setting

	PALOMA-2[1]	MONALEESA-2[2]	MONARCH 3[3]	MONALEESA-3[4‡]
All patients	Palbociclib + letrozole (n=444) versus placebo + letrozole (n=222)	Ribociclib + letrozole (n=334) versus placebo + letrozole (n=334)	Abemaciclib + NSAI (n=328) versus placebo + NSAI (n=165)	First-/second-line: Ribociclib + fulvestrant (n=238/236) versus placebo + fulvestrant (n=129/109)
Overall response rate (ORR)*, % (95% CI)	**42.1** (37.5–46.9) versus **34.7** (28.4–41.3)	**42.5** (37.2–47.8) versus **28.7** (23.9–33.6)	**48.2** (42.8–53.6) versus **34.5** (27.3–41.8)	**32.4** (28.3–36.6) versus **21.5** (16.3–26.7)
Clinical benefit rate (CBR)†, % (95% CI)	**84.9** (81.2–88.1) versus **70.3** (63.8–76.2)	**79.9** (75.6–84.2) versus **73.1** (68.3–77.8)	**78.0** (73.6–82.5) versus **71.5** (64.6–78.4)	**70.2** (66.2–74.3) versus **62.8** (56.7–68.9)

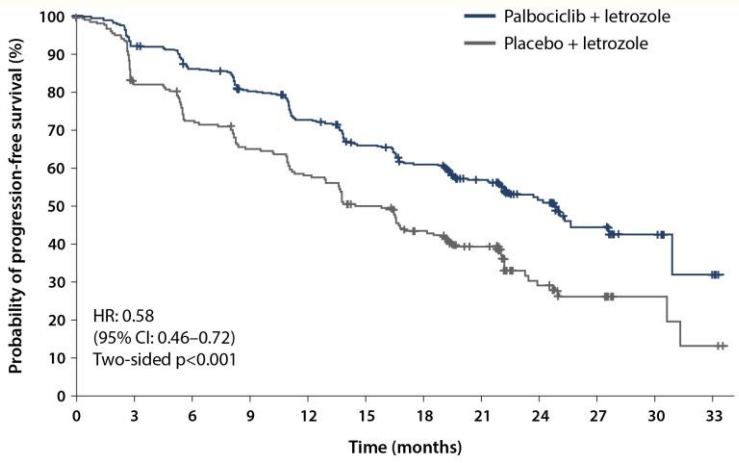
This table is intended to be a summary of the available clinical trials only and direct comparisons cannot be made.
‡ Results for MONALEESA-3 are not specific to first-line treatment.

* ORR = complete response (CR) + partial response (PR). † CBR = CR + PR + (stable disease/neither complete response nor progressive disease ≥24 weeks).

1. Finn et al. *The New England Journal of Medicine*. 2016;375(20):1925-1936. 2. Hortobagyi et al. *Annals of Oncology*. 2018;29(7):1541-1547. 3. Goetz et al. *Journal of Clinical Oncology*. 2017;35(32):3638-3646. 4. Slamon et al. *Journal of Clinical Oncology*. 2018;36:2465-2472.

PALOMA-2 Primary Endpoint: PFS

Investigator-assessed PFS in the ITT population: Primary analysis[1]*



An updated PALOMA-2 analysis showed:[2†]

HR: 0.56
(95% CI: 0.46–0.69); p<0.0001

Median PFS difference: 13.1 months
Palbociclib + letrozole: 27.6 months (95% CI: 22.4–30.3)
Placebo + letrozole: 14.5 months (95% CI: 12.3–18.5)

In patients with bone-only disease:[2†]

HR: 0.41 (95% CI: 0.26–0.63; p<0.0001)
Median PFS difference: 25 months
Palbociclib + letrozole (n=103): 36.2 months (95% CI: 27.6–NE)
Placebo + letrozole (n=43): 11.2 months (95% CI: 8.2–22.0)

NE: Not estimable.
* Median follow-up was 23 months. † Median follow-up was 38 months for palbociclib + letrozole and 37 months for placebo + letrozole.
1. Finn et al. *The New England Journal of Medicine*. 2016;375(20):1925-1936. 2. Rugo et al. *Breast Cancer Research and Treatment*. 2019;174(3):719-729.

PALOMA-2: Adverse Event

Most common adverse events in the palbociclib + letrozole treatment group (≥25% occurrence)[1]

Adverse event, n (%)	Palbociclib + letrozole (n=448)			Placebo + letrozole (n=222)*		
	Any Grade	Grade 3	Grade 4†	Any Grade	Grade 3	Grade 4
Any adverse event	439 (98.9)	276 (62.2)	60 (13.5)	212 (95.5)	49 (22.1)	5 (2.3)
Neutropenia‡	**353 (79.5)**	**249 (56.1)**	**46 (10.4)**	**14 (6.3)**	**2 (0.9)**	**1 (0.5)**
Leukopenia§	**173 (39.0)**	**107 (24.1)**	**3 (0.7)**	**5 (2.3)**	**0**	**0**
Fatigue	166 (37.4)	8 (1.8)	0	61 (27.5)	1 (0.5)	0
Nausea	156 (35.1)	1 (0.2)	0	58 (26.1)	4 (1.8)	0
Arthralgia	148 (33.3)	3 (0.7)	0	75 (33.8)	1 (0.5)	0
Alopecia¶	146 (32.9)	0	0	35 (15.8)	0	0
Diarrhea	116 (26.1)	6 (1.4)	0	43 (19.4)	3 (1.4)	0
Cough	111 (25.0)	0	0	42 (18.9)	0	0

* One death secondary to lower respiratory tract infection and pulmonary embolism occurred in the placebo–letrozole group and was believed to be treatment related. † Grade 4 events that were reported in the palbociclib–letrozole group but not shown in the table were increased alanine aminotransferase level, increased blood creatinine level, febrile neutropenia, pulmonary embolism, acute kidney injury, hyperuricemia, acute pancreatitis, pathologic fracture, pericardial effusion, sepsis, increased amylase level, aortic valve stenosis, pulmonary edema, staphylococcal bacteremia, thrombotic cerebral infarction, urosepsis, and increased lipase level; these grade 4 events were reported in one patient each, except for increased lipase level, which was reported in two patients. ‡ Neutropenia was categorized according to the *Medical Dictionary for Regulatory Activities* (MedDRA) preferred terms neutropenia and neutrophil count decreased. Febrile neutropenia was reported in 1.8% of patients in the palbociclib–letrozole group and in no patients in the placebo–letrozole group. § Leukopenia was categorized according to the MedDRA preferred terms leukopenia and white blood cell count decreased. ¶ In the palbociclib–letrozole group, 30.2% of the patients had grade 1 alopecia and 2.7% had grade 2. In the placebo–letrozole group, 14.9% of patients had grade 1 alopecia and 0.9% had grade 2.

1. Finn et al. *The New England Journal of Medicine*. 2016;375(20):1925-1936.

Local Resources

- **WRCC Call Centre:** (519) 253-5253
- **Dedicated line for providers:** 519-255-6757
- Breast Assessment Programs: BWH, CKHA, ESHC & WRH
- Surveillance/Survivorship Guides (in your packages)
- Local Breast Oncologists

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References

- Cancer Care Ontario – Breast Cancer: https://www.cancercareontario.ca/en/types-of-cancer/breast-cancer
- Canadian Cancer Society – Breast Cancer: http://www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/?region=on
- Erie St. Clair Regional Cancer Program: www.wrh.on.ca/cancerprogram

THANKS