

# BC Cancer Protocol Summary for Therapy of Advanced Breast Cancer using Palbociclib and Aromatase Inhibitor With or Without LHRH Agonist

**Protocol Code**

*BRAVPALAI*

**Tumour Group**

*Breast*

**Contact Physician**

*Dr. Sophie Sun*

## **ELIGIBILITY:**

Patients must:

- Have ER-positive, HER2-negative advanced or metastatic breast cancer,
- Be post-menopausal women (including women with chemically induced menopause with LHRH agonists), or men,
- Have no prior endocrine treatment for advanced or metastatic disease, but may have up to one prior line of chemotherapy,
- Not be resistant to prior (neo) adjuvant aromatase inhibitor therapy (patients must be a minimum of 12 months from last adjuvant aromatase inhibitor), and
- Not be resistant to prior adjuvant abemaciclib (patients must be a minimum of 6 months from completion of adjuvant abemaciclib)

Patients should have:

- Good performance status

Notes:

- Patients are eligible to receive any of the following, but not their sequential use:
  - Palbociclib plus fulvestrant (BRAVPBFLV) or ribociclib plus fulvestrant (BRAVRBFLV),  
OR
  - Ribociclib plus letrozole/anastrozole (BRAVRIBAI) or palbociclib plus letrozole/anastrozole (BRAVPALAI)  
OR
  - Everolimus plus exemestane (BRAVEVEX)
- For patients recently diagnosed with metastatic breast cancer, and who have initiated anastrozole or letrozole monotherapy within the past 6 months, palbociclib can be added if the rest of the above criteria are met.

## **EXCLUSIONS:**

Patients must not have:

- Active or uncontrolled metastases to the central nervous system,
- Advanced symptomatic and life-threatening visceral metastases,
- Pregnant women,
- Palbociclib monotherapy

## **CAUTIONS:**

- Severe hepatic dysfunction
- Severe renal impairment

**TESTS:**

- Baseline: CBC and differential, platelets, creatinine, ALT, alkaline phosphatase, total bilirubin, GGT, LDH
- Baseline if indicated: CA15-3, ECG
- Cycles 1 to 6 of palbociclib:
  - Prior to Day 1 of each cycle: CBC and differential, platelets, creatinine
  - On Day 15 of cycle 1: CBC and differential, platelets
  - On Day 15 of cycle 2 (if clinically indicated; for dose adjustment or delay in cycle 1): CBC and differential, platelets
  - On Day 22 of cycle 1 and 2 if Day 15 ANC 0.5 to less than  $1.0 \times 10^9/L$ : CBC and differential, platelets
- Cycles 7 onwards of palbociclib:
  - If ANC  $1.0 \times 10^9/L$  or higher during first 6 cycles:
    - Prior to every third cycle: CBC and differential, platelets, creatinine
  - If ANC less than  $1.0 \times 10^9/L$  during first 6 cycles:
    - Prior to each cycle: CBC and differential, platelets, creatinine
- If clinically indicated: ALT, alkaline phosphatase, total bilirubin, GGT, LDH, CA15-3, ECG, serum cholesterol, triglycerides

**PREMEDICATIONS:**

- Not usually required

**TREATMENT:**

Until disease progression or unacceptable toxicity

Drug	Dose	BC Cancer Administration Guideline
palbociclib	125 mg once daily for 21 days on, 7 days off (one cycle = 28 days)*	PO
<b>Plus Aromatase Inhibitor</b>		
letrozole	2.5 mg once daily continuously	PO
OR		
anastrozole	1 mg once daily continuously	PO

\* Repeat palbociclib every 28 days (One cycle = 28 days).

- If a dose is missed, take the **next** dose at the same usual time.
- If palbociclib is resumed after being held due to toxicity:
  - Stop on Day 21 as scheduled
  - Maintain at least 7 days rest before resuming next cycle.

**For women needing chemically induced menopause and male patients:**

<b>Drug</b>	<b>Dose</b>	<b>BC Cancer Administration Guideline</b>
goserelin long acting (ZOLADEX)**	3.6 mg every 4 weeks	subcutaneous
OR		
leuprolide long acting (LUPRON DEPOT)**	7.5 mg every 4 weeks	IM

\*\*Once response has been established, the following long-acting agents may be substituted at the physician's discretion. In women, menstrual function, and if necessary, hormone levels can be monitored to ensure effective dosing.

<b>Drug</b>	<b>Dose</b>	<b>BC Cancer Administration Guideline</b>
goserelin long acting (ZOLADEX LA)*	10.8 mg every 12 weeks	subcutaneous
OR		
leuprolide long acting (LUPRON DEPOT)*	22.5 mg every 12 weeks	IM

## DOSE MODIFICATIONS:

### Palbociclib dose level

Dose level	Daily dose
Starting dose	125 mg
First dose reduction	100 mg (should not re-escalate to 125 mg)
Second dose reduction	75 mg* (may re-escalate to 100 mg at physician's discretion)

\* Discontinue if further dose reduction required below 75 mg per day.

### 1. Hematological – for Palbociclib

No hematological dose modifications for aromatase inhibitor or LHRH agonist (if using)

Neutropenia (ANC x10 <sup>9</sup> /L)	Palbociclib Dose Modifications
Grade 1 and 2 (greater than or equal to 1.0)	Continue at same dose.
Grade 3 (0.5 to less than 1.0)*	<u>Day 1</u> Delay. If ANC greater than or equal to 1.0 x 10 <sup>9</sup> /L within 1 week, resume at same dose.
	<u>Day 15 of cycles 1 and 2</u> Continue same dose for remainder of cycle. Check ANC on Day 22; If ANC on Day 22 is: <ul style="list-style-type: none"><li>greater than or equal to 0.5 x 10<sup>9</sup>/L: continue at same dose for next cycle, when ANC greater than or equal to 1.0 x 10<sup>9</sup>/L</li><li>less than 0.5 x 10<sup>9</sup>/L: resume at next lower dose, when ANC greater than or equal to 1.0 x 10<sup>9</sup>/L</li></ul>
Grade 4 (less than 0.5) OR Grade 3 plus fever and/or infection	<u>Day 1</u> Delay. When ANC greater than or equal to 1.0 x 10 <sup>9</sup> /L, resume at next lower dose.
	<u>Day 15 of cycles 1 and 2</u> Omit remainder of cycle. When ANC greater than or equal to 1.0 x 10 <sup>9</sup> /L, resume at next lower dose.

Thrombocytopenia (Platelets x10 <sup>9</sup> /L)	Palbociclib Dose Modifications
Grade 1 and 2 (greater than or equal to 50)	Continue at same dose.
Grade 3 (25 to 49) and Grade 4 (less than 25) *	<u>Day 1</u> Delay. When greater than or equal to 50 x 10 <sup>9</sup> /L, resume at next lower dose.
	<u>Day 15 of cycles 1 and 2</u> Omit remainder of cycle. When platelets greater than or equal to 50 x 10 <sup>9</sup> /L, resume at next lower dose.

\*Consider dose reduction if more than 1 week to recover, or recurrent on Day 1 of subsequent cycles.

**PRECAUTIONS:**

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal dysfunction:** palbociclib has not been studied in patients with creatinine clearance less than 15 mL/min.
3. **Hepatic dysfunction:** No dose adjustment is required for mild or moderate hepatic impairment (Child-Pugh classes A and B). For patients with severe hepatic impairment (Child-Pugh class C), use 75 mg PO once daily for 21 consecutive days in a 28 day cycle.
4. **Drug-drug interactions:** palbociclib is metabolized via CYP3A enzymes. Concurrent use of CYP3A inhibitors, substrates or inducers may affect palbociclib serum level.

**Call Dr. Sophie Sun or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

**References:**

1. Finn RS, et al. Palbociclib and letrozole in advanced breast cancer. N Engl J Med 2016;375:1925-36.
2. Finn RS, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol 2015;16:25-35.
3. Pfizer Canada Inc. IBRANCE® product monograph. Kirkland, Quebec; 24 January 2020.