

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

**Protocol Code**

**BRAVPBFLV**

**Tumour Group**

**Breast**

**Contact Physician**

**Dr. Stephen Chia**

## ELIGIBILITY:

Patients must be:

- Post-menopausal women (including women with chemically induced menopause with LHRH agonists) and men with ER-positive, HER2-negative advanced or metastatic breast cancer, and
- may have received any lines of prior endocrine (except fulvestrant) and up to one prior line of chemotherapy for advanced or metastatic disease. This includes patients whose disease progressed:
  - On (neo) adjuvant endocrine therapy,
  - Within 12 months of completing adjuvant endocrine therapy, or
  - On or after endocrine therapy for advanced or metastatic disease.

Notes:

- Patients should have good performance status

*\* Note: 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).*

*Patients who have received the above regimens are NOT eligible for subsequent use of everolimus plus exemestane (BRAVEVEX).*

*\*\* Note: For patients recently diagnosed with metastatic breast cancer, and who have initiated fulvestrant monotherapy within the past 6 months, palbociclib can be added if the rest of the above criteria are met.*

## EXCLUSIONS:

- Patients should 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 (total bilirubin greater than 50 micromol/L)
- Severe renal impairment (calculated creatinine clearance less than 30 mL/min)

**TESTS:**

- Baseline: CBC & diff, platelets, creatinine, ALT, alkaline phosphatase, total bilirubin, GGT, LDH
- Baseline if indicated: CA15-3, ECG
- Cycles 1 and 2 of palbociclib
  - Prior to day 1 of each cycle: CBC & diff, platelets, creatinine
  - On day 15: CBC & diff, platelets
- Cycles 3 to 6 of palbociclib
  - Prior to each cycle: CBC & diff, platelets, creatinine
- 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 & diff, platelets, creatinine
  - If ANC less than  $1.0 \times 10^9/L$  during first 6 cycles:
    - Prior to each cycle: CBC & diff, 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</b>		
fulvestrant Cycle 1	500 mg once on days 1 and 15	IM (Administer as two 250 mg injections)
**fulvestrant Cycle 2 onwards	500 mg once every 28 days $\pm$ 3 days	IM (Administer as two 250 mg injections)

\* Repeat palbociclib every 28 days. If a dose is missed, take the **next** dose at the same usual time. If a dose is held due to toxicity, patient should stop on day 21 of the original schedule when resuming dose to maintain the 1-week rest.

\*\*In case palbociclib is delayed/held/omitted, fulvestrant treatment should be continued as planned.

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

<b>Drug</b>	<b>Dose</b>	<b>BC Cancer Administration Guideline</b>
buserelin long acting (SUPREFACT DEPOT)*	6.3 mg every 6 weeks x 2 treatments then every 8 weeks	subcutaneous
OR		
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>
buserelin long acting (SUPREFACT DEPOT)*	9.45 mg every 12 weeks	subcutaneous
OR		
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/d
First dose reduction	100 mg/d (should not re-escalate to 125 mg/d)
Second dose reduction	75 mg/d* (may re-escalate to 100 mg/d at physician's discretion)

\* Discontinue if further dose reduction required below 75 mg/d

### 1. Hematological

Neutropenia (ANC x10 <sup>9</sup> /L)	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 ≥ 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)	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. Stephen Chia or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

**References:**

1. Slamon DJ et al. Overall Survival with Ribociclib plus Fulvestrant in Advance Breast Cancer. N Engl J Med. 2020 Feb 6;382(6):514-524.
2. Sledge GW et al. The Effect of Abemaciclib Plus Fulvestrant on Overall Survival in Hormone Receptor–Positive, ERBB2-Negative Breast Cancer That Progressed on Endocrine Therapy—MONARCH 2. JAMA Oncol. 2020;6(1):116-124.
3. Turner NC et al. Overall Survival with Palbociclib and Fulvestrant in Advanced Breast Cancer. N Engl J Med. 2018 Nov 15;379(20):1926-1936.