Regimen Reference Order – BRST - ribociclib + fulvestrant +/- goserelin

ARIA: BRST – [ribociclib]
BRST – [fulvestrant]
BRST – [LHRH Agonists]

Planned Course: **Until disease progression or unacceptable toxicity (1 cycle of ribociclib = 28 days)**

Indication for Use: **Breast Cancer Metastatic, Hormone Receptor Positive, HER2 negative**

CVAD: Not Required

Proceed with treatment if:

ribociclib

- ***ANC equal to or greater than 1 x 10^9/L AND Platelets equal to or greater than 75 x 10^9/L***

fulvestrant and LHRH agonist

- ***Continued throughout therapy regardless of CBC. If ribociclib is held for toxicity, fulvestrant and LHRH agonist are continued***
  - ❖ **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – BRST – ribociclib + fulvestrant +/- goserelin

Drug	Dose	CCMB Administration Guideline
ribociclib	600 mg	Orally once daily on **Days 1 to 21, then 7 days off** Take with or without food Swallow whole **(Self-administered at home)**
fulvestrant	500 mg (2 syringes of 250 mg)	**With Cycle 1 of ribociclib:** Intramuscular into ventrogluteal muscle over 1 to 2 minutes per injection (administer 500 mg dose as two 5 mL IM injections) on **Days 1 and 15**
		Starting 4 weeks after first dose of fulvestrant: Intramuscular into ventrogluteal muscle over 1 to 2 minutes per injection (administer 500 mg dose as two 5 mL IM injections) **(fulvestrant administered once every 28 days)**
goserelin* **OR** alternate LHRH agonist* (see options on table on Page 3)	3.6 mg	Subcutaneous once every 28 days **(goserelin or alternate LHRH agonist starts 28 days prior to the start of fulvestrant then continues throughout therapy)**

* LHRH agonists are only prescribed for pre- or peri-menopausal patients

ribociclib (Kisqali®) available dosage strength: 200 mg tablet
Classification: Cytotoxic, Hazardous

fulvestrant (Faslodex®) available dosage strength: 250 mg per 5 mL syringe
Classification: Non-Cytotoxic, Hazardous

In the event of an infusion-related hypersensitivity reaction, refer to the '**Hypersensitivity Reaction Standing Order**'

REQUIRED MONITORING

For ribociclib

Cycles 1 and 2

- CBC and biochemistry (including liver enzymes and total bilirubin) prior to Days 1 and 15 as per Physician Orders

Cycles 3 to 6

- CBC and biochemistry (including liver enzymes and total bilirubin) prior to Day 1 and as clinically indicated as per Physician Orders
- No blood work required on Day 15

Cycle 7 and Onwards

- CBC prior to Day 1 at physician's discretion
  - Each cycle (if ANC was less than 1 x 10^9/L during first 6 cycles) or
  - Every 3rd cycle (if ANC was 1 x 10^9/L or greater during first 6 cycles)
- Biochemistry (including liver enzymes and total bilirubin) periodically as clinically indicated as per Physician Orders

EKG monitoring

- Prior to initiation of treatment, then
- Cycle 1, Day 14, then
- Cycle 2, Day 1, then
- at regular intervals thereafter during steady-state treatment (at approximately Day 14 of the cycle) and whenever clinically indicated

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
None required		

DISCHARGE INSTRUCTIONS

- ribociclib has potential for drug-drug interactions. Patients should notify clinic prior to starting any new medication
- ribociclib has potential for myelosuppression
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade), and starfruit with ribociclib
- Reinforce applicable safe handling precautions of medications, blood and body fluids while on ribociclib

ADDITIONAL INFORMATION

- The length of the needle provided with fulvestrant is 1.5 inches (38 mm)
- The patient's body habitus and ventrogluteal fat thickness should be evaluated to ensure the delivery of drug into the muscle
- The preferred site of administration for fulvestrant is into ventrogluteal muscle. Dorsogluteal injections are associated with increased possibility of damaging the sciatic nerve
- fulvestrant should be kept in the refrigerator
- QT prolongation has been associated with ribociclib; dose interruptions and/or reductions may be required for QT prolongation
- Breast DSG oncologists may prescribe ribociclib in combination with different LHRH agonists
- Pre- and peri-menopausal patients initiate LHRH agonist therapy at least 4 weeks before starting treatment with ribociclib and fulvestrant
- Due to the various combinations used with ribociclib, this Regimen Reference Order provides only one example of possible combinations. The table below outlines different drugs/dosing schedules which may be prescribed:

Options for LHRH Agonists

Drug	Dose	CCMB Administration Guideline
goserelin	3.6 mg	Subcutaneous once every 28 days (4 weeks)
	OR	
	10.8 mg	Subcutaneous once every 84 days (12 weeks)
OR		
leuprolide	7.5 mg	Subcutaneous once every 28 days (4 weeks)
	OR	
	22.5 mg	Subcutaneous once every 84 days (12 weeks)

goserelin (Zoladex®) available dosage strengths: 3.6 mg, 10.8 mg syringe
Classification: Non-Cytotoxic, Hazardous

leuprolide (Eligard®) available dosage strengths: 7.5 mg, 22.5 mg syringe
Classification: Non-Cytotoxic, Hazardous

- ribociclib dose interruptions and/or reductions may be required for neutropenia; If ribociclib is held for toxicity reasons, fulvestrant and LHRH agonist therapy continue while ribociclib is held
- Please note that ARIA regimens/protocols require each drug to be ordered separately
    - **BRST – [ribociclib]** regimen is available as a 28-day cycle under the "Breast" treatment tab in ARIA
    - Support protocol is available for **fulvestrant** under **BRST – [fulvestrant]**
    - Support protocols are available for **goserelin** and **leuprolide** (either q 4 weeks OR q 12 weeks) under **BRST – [LHRH Agonists]**
- ribociclib will be dispensed by CCMB Pharmacy