OPTUMRx

Class Quick Reference
Oncology

INTRODUCTION

- Breast cancer is the most frequently diagnosed cancer globally and is the leading cause of cancer-related death in women. Long-term survival outcomes are related to disease stage at diagnosis *(National Comprehensive Cancer Network [NCCN] 2017)*.
  - o Most patients presenting with localized disease will have long-term disease-free survival (*Rugo et al 2016*).
  - o Systemic treatment of breast cancer recurrence or metastatic disease prolongs survival and quality of life, but is generally not curative. Treatments associated with minimal toxicity are preferred *(Rugo et al 2016, NCCN 2017).*
- Biologic markers such as hormone receptor (HR) status (estrogen receptor [ER] and progesterone receptor [PR] status), human epidermal growth factor receptor 2 (HER2) overexpression, and tumor burden have both prognostic and predictive value of treatment response. Treatment selection should be based upon these markers *(UpToDate 2017).*
- Chronic myelogenous leukemia (CML) is an uncommon type of cancer of the blood cells.
- Afinitor is a kinase inhibitor of mammalian target of rapamycin (mTOR), a serine-threonine kinase, downstream of the PI3K/AKT pathway.
- Ibrance is an inhibitor of cyclin-dependent kinases (CDK) 4 and 6.
- Sprycel is a kinase inhibitor for: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGRFβ.

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Afinitor® (Everolimus)	–
Ibrance® (Palbociclib)	–
Sprycel® (Dasatinib)	–

(*Drugs@FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018*)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Everolimus	Palbociclib	Dasatinib
Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.	X		
Adults with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic.	X		
Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.	X		
Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.	X		
Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine based therapy in postmenopausal women; or • fulvestrant in women with disease progression following endocrine therapy.		X	
Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.			X
Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.			X
Adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.			X
Pediatric patients with Ph+ CML in chronic phase			X

(*Prescribing information: Afinitor 2018, Ibrance 2018, Sprycel 2018*)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL GUIDELINES

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines: Breast Cancer (v2.2017)**
  - For initial treatment of postmenopausal patients with ER-positive, HER2-negative, recurrent or metastatic disease, NCCN recommends aromatase inhibitors (anastrozole or letrozole), serum ER modulators (tamoxifen or toremifene), selective ER down-regulator (fulvestrant), progestin, androgens, high-dose estrogen, or newer combination therapies (see Table 4 for a complete list of recommended regimens).
    - The combination of palbociclib or ribociclib with letrozole is included as a category 1, first-line endocrine therapy option for postmenopausal women with HR-positive, HER2-negative metastatic breast cancer.
    - The combination of palbociclib with fulvestrant is included as a category 1 option for premenopausal women receiving ovarian suppression or postmenopausal women with HR-positive, HER2-negative metastatic breast cancer who have progressed on endocrine therapy.
  - Women who respond to endocrine therapy should receive additional endocrine therapy at disease progression. Chemotherapy should be reserved for patients who have demonstrated no clinical benefit after 3 sequential endocrine therapy regimens or those with symptomatic visceral disease.

- **American Society of Clinical Oncology (ASCO) Clinical Practice Guideline: Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer *(Rugo et al 2016)***
  - Sequential hormone therapy is the preferential treatment for most women with HR-positive metastatic breast cancer. Except in cases of immediately life-threatening disease, hormone therapy, alone or in combination, should be used as initial treatment.
  - For postmenopausal women, aromatase inhibitors are the preferred first-line treatment, with or without palbociclib.
  - Premenopausal women should be offered ovarian suppression or ablation and hormone therapy; current hormonal agents have not been studied in premenopausal women.
  - Fulvestrant plus palbociclib may be utilized in pre- or postmenopausal patients experiencing progression during prior treatment with aromatase inhibitors with or without 1 line of prior chemotherapy.
  - Sequential hormone therapy should be offered to patients with endocrine-responsive disease, except in the case of rapid progression with organ dysfunction; no specific order of agents is recommended.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Afinitor	Tablets: 2.5mg 5mg 7.5mg 10mg Disperz: 2mg 3mg 5mg	PO	Breast Cancer, NET, RCC: 10mg PO once daily	Also used for certain seizure disorders.
Ibrance	Capsules: 125mg 100mg 75mg	PO	125mg PO once daily	Taken with food. Given for 21 days followed by 7 days off treatment.
Sprycel	Tablets: 20mg 50mg 70mg 80mg 100mg 140mg	PO	Adults: Chronic Phase CML: Starting 100mg PO once daily Others: Starting 140mg PO once daily Pediatric: Based on body weight	Follow dose escalation per package insert. Tablets must be swallowed whole, do not crush, cut or chew. Adjustment necessary for Strong CYP3A4 Inducers and Inhibitors.

REFERENCES

- Ibrance [package insert], New York, NY: Pfizer; September 2018
- Afinitor [package insert], East Hanover, NJ: Novartis, April 2018
- Sprycel [package insert], Princeton, NJ: Bristol-Myers Squibb Company; November 2018
- Rugo HS, Rumble RB, Macrae E, et al. Endocrine therapy for hormone receptor-positive metastatic breast cancer: American Society of Clinical Oncology Guideline. *J Clin Oncol*. 2016; 34:3069-103.
- National Comprehensive Cancer Network Clinical Practice Guideline: Breast Cancer (v.2.2017). http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 11, 2017.