

## **Diagnostic Work-Up**

**Clinical suspicion based on palpable mass** 

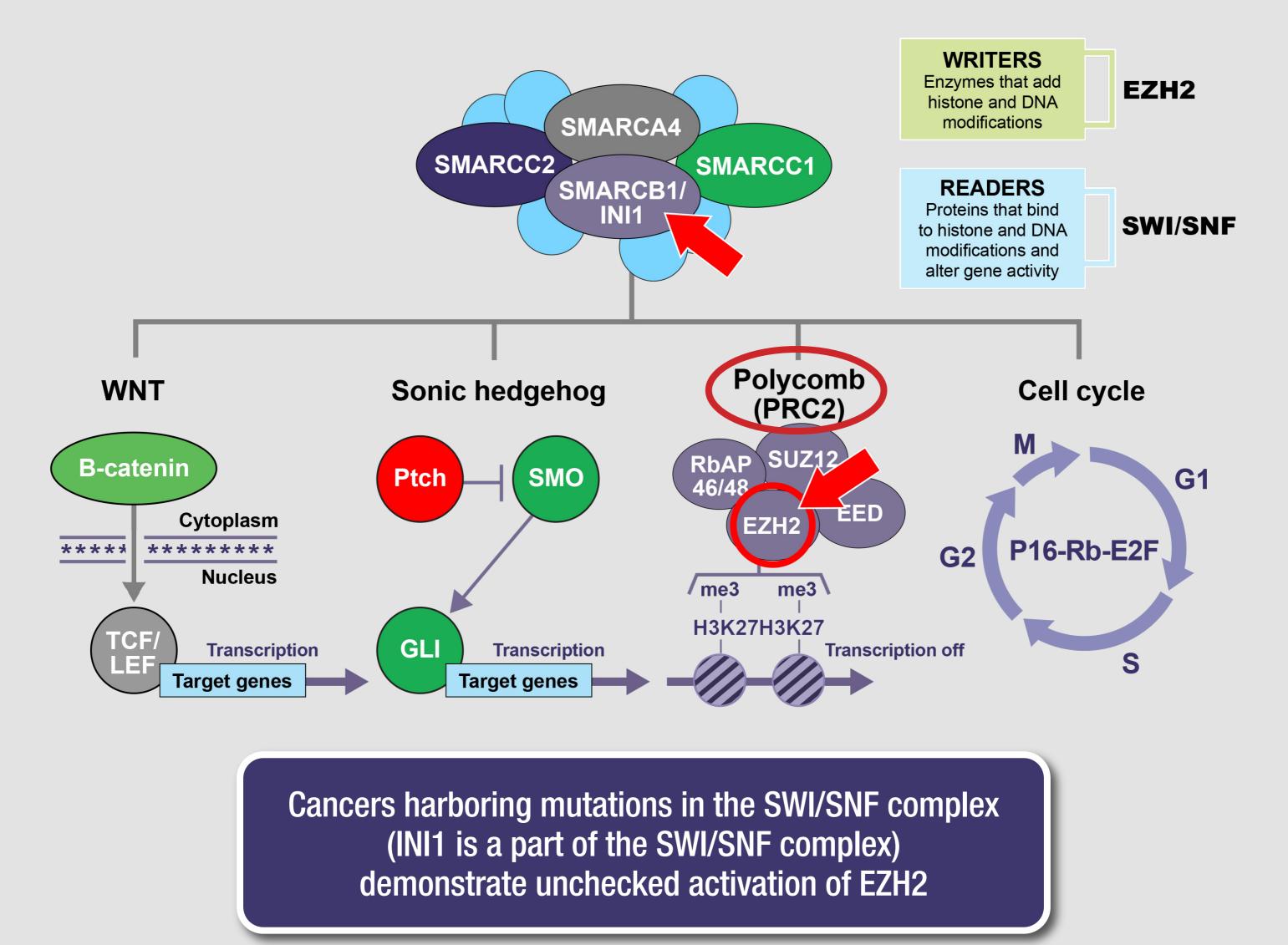
### Imaging to determine anatomic boundaries

### Core biopsy and pathologic analysis

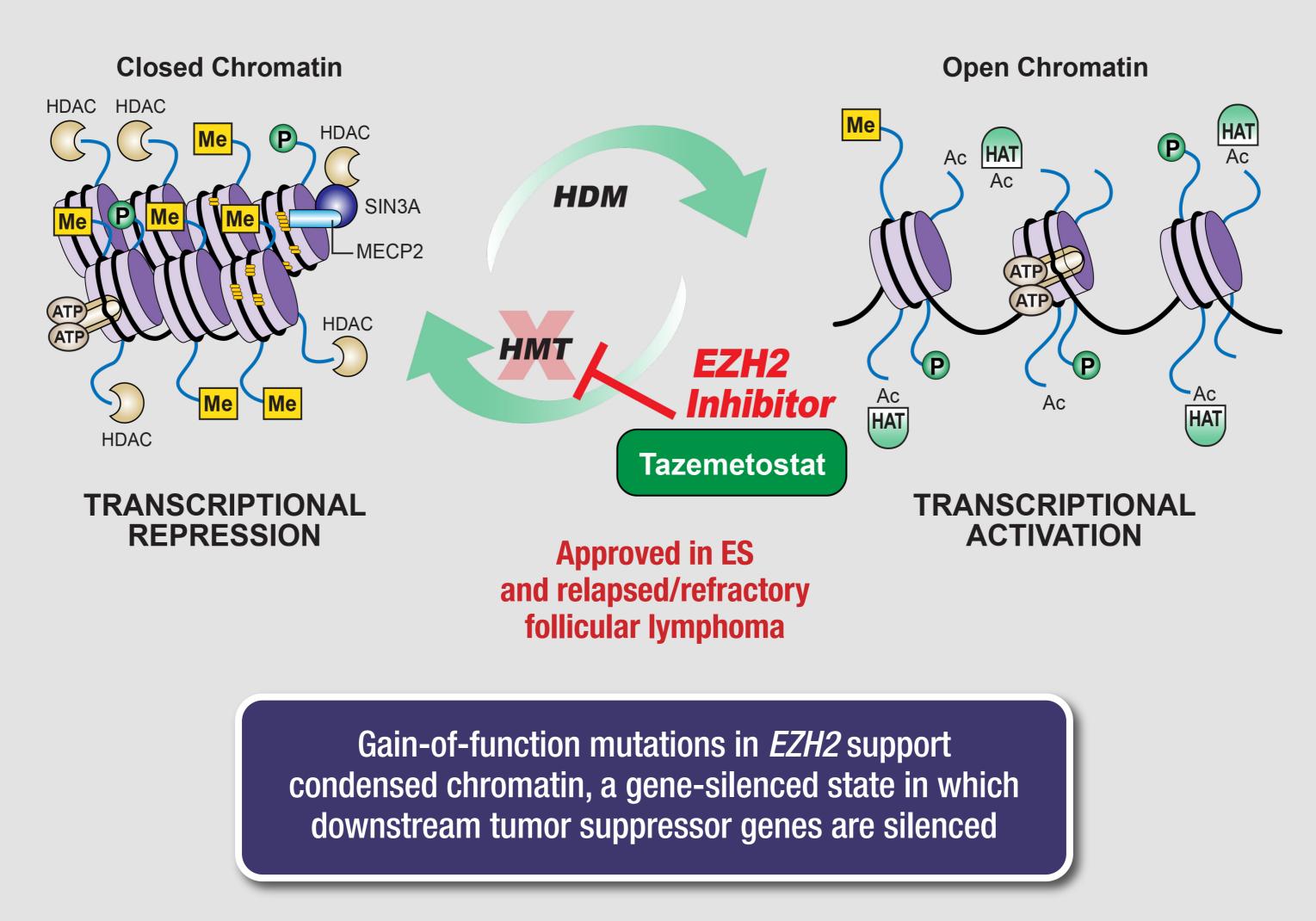
- Histopathologic assessment
- IHC staining to assess INI1 expression loss

## **EPIGENETICS IN THE PATHOLOGY AND TREATMENT OF ES**

### **Roles of INI1 and EZH2 in ES**

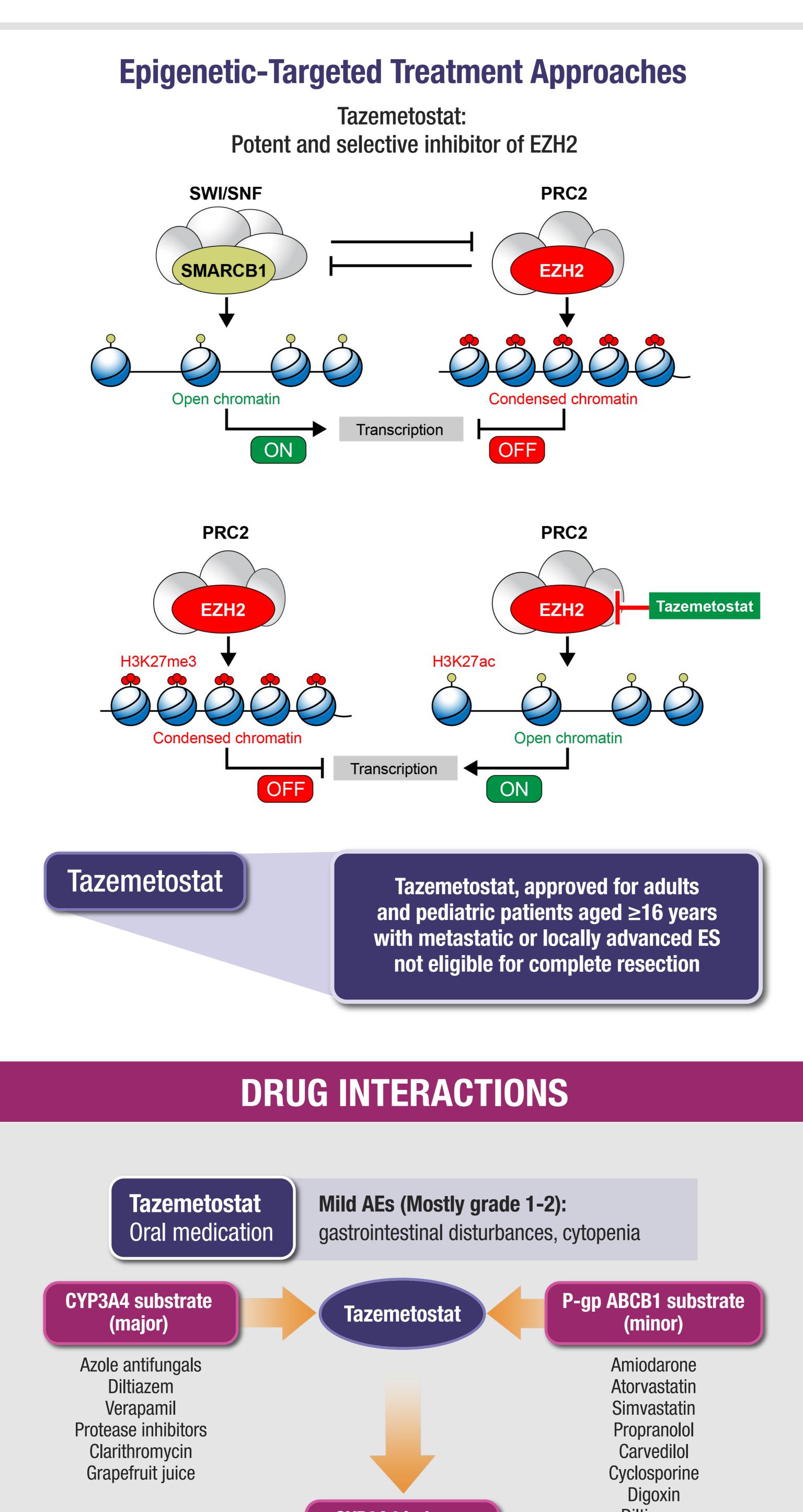


## **EZH2 Inhibitors: Mechanism of Action**



# **SELECTING TREATMENT STRATEGIES FOR ES**

- Treatment may involve surgery, radiation, chemotherapy, and/or an interventional procedure
- Surgery is the only curative therapy, but most patients have surgically incurable disease burden by the time of diagnosis
- Systemic treatments are mainstay of treatment in metastatic setting; most common first-line chemotherapeutic options include anthracycline-based regimens, gemcitabine-based regimens, or pazopanib, especially in those with rapidly growing tumors





CYP3A4 inducer (weak)

#### **Dosing Considerations With DDIs**

Concurrent use with strong or moderate CYP3A4 inhibitors is discouraged. If a moderate CYP3A4 inhibitor must be used, follow these dosing recommendations:

Currently Administered Dose	Dose Adjustments for Moderate CYP3A4 Inhibitors
800 mg twice daily	400 mg twice daily
600 mg twice daily	400 mg in the morning and 200 mg in the evening
400 mg twice daily	200 mg twice daily

No data are currently available to recommend dose adjustments for concomitant CYP3A4 inducers

- Don't forget to resume normal tazemetostat dosing if the offending agent is discontinued!
- If CYP3A4 inhibitor dosing can be adjusted or discontinued, try this first to avoid diminishing the efficacy of tazemetostat at the recommended full dose

## **MULTIDISCIPLINARY AND MULTIFACETED CARE**

Clinical practice guidelines recommend that the treatment of patients with sarcoma be managed by dedicated multidisciplinary teams



## Pharmacists as a Part of the ES Care Team



- Determining when EZH2 inhibition is an appropriate treatment
- Pharmacotherapy management: AEs, tolerability, DDIs, adherence
- Patient/caregiver education about new therapies
- Assisting with medication access

AE: adverse event; DDI: drug-drug interaction; EZH2: enhancer of zeste homolog 2; h3K27: histone 3, lysine 27; HMT: histone methyltransferase; INI1: integrase interactor 1; me3: trimethylated; PRC2: polycomb repressive complex 2; SMARCB1: SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1; SWI/SNF: switch/sucrose non-fermentable.

#### References

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