JADPRO Clinical Case Series

Treatment Selection and Adverse Event Management in Follicular Lymphoma

SUPPORTED BY

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PRESENTER

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Program Agenda

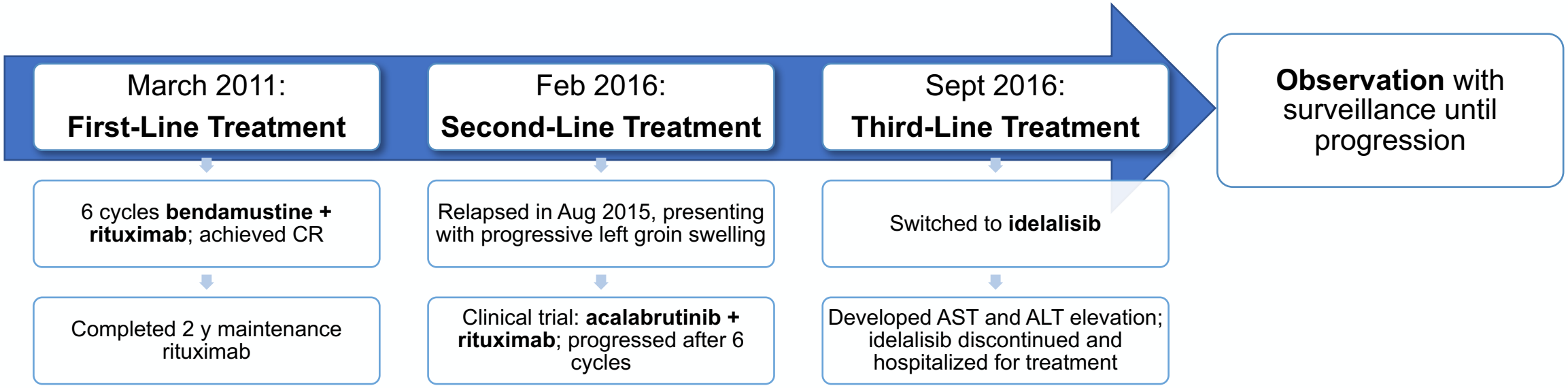
- Review the role of targeted therapies in the later lines of treatment among patients with follicular lymphoma (FL) and the overall management of these patients
- Discuss the management of potential adverse events (AEs) that can occur with targeted therapies
- Examine case studies to gain a better understanding of treatment decision-making and management of AEs in FL, and the role of a multidisciplinary team approach

Case 1

Introduction to Case 1: Relapsed FL

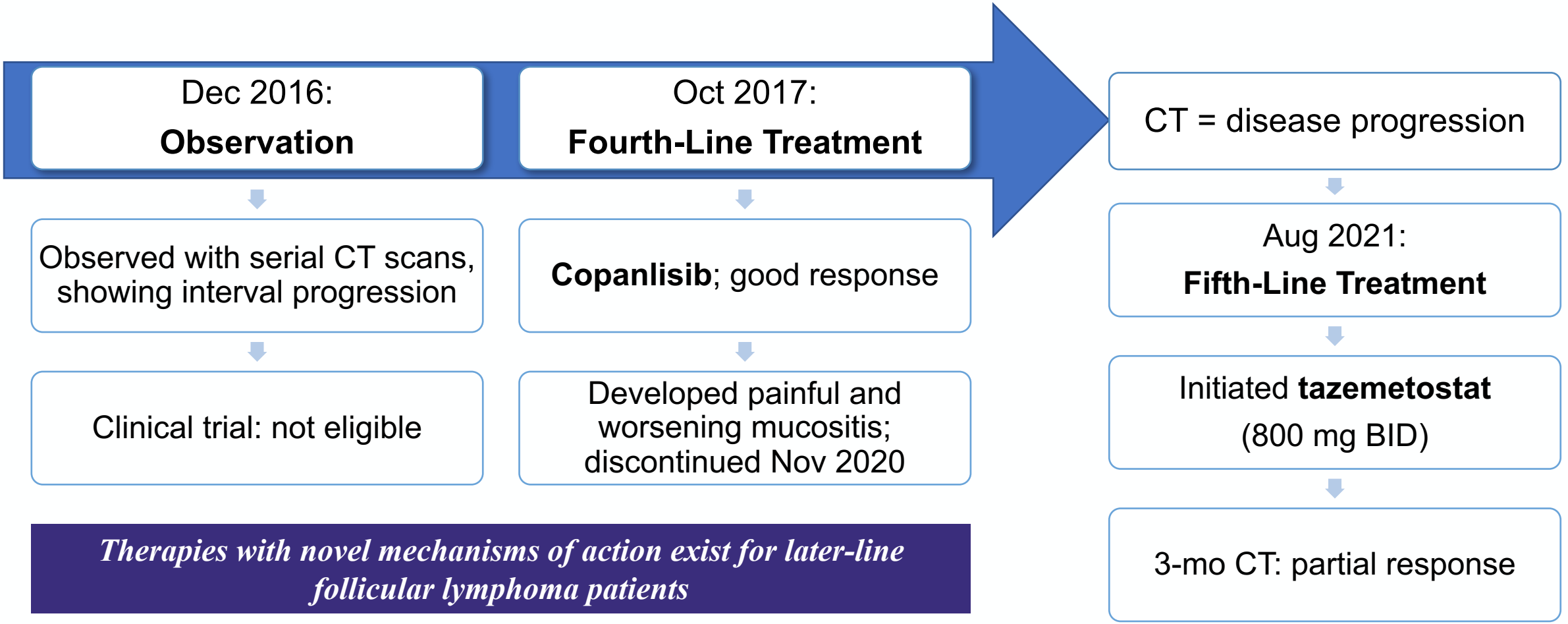
Mr. Kay is a 56-year-old man who was diagnosed with FL in March 2011

- Stage IV with bone marrow involvement



ALT, alanine transaminase; AST, aspartate transaminase; CR, complete remission

Case 1: Subsequent Treatment Selection



Polling Question

For patients with FL in their third line of treatment or beyond, which of the following considerations guides your treatment selection most strongly?

A. Switching to a medication with a different mechanism of action than the medications the patient has already received **55%**

B. Re-using an agent (i.e., rituximab) that has provided benefit in the past **27%**

C. Selecting a treatment based on logistical concerns, such as route of administration or dosing schedule **18%**

Improved Prognosis in the New Treatment Era

FL typically thought of as chronic disease[1]

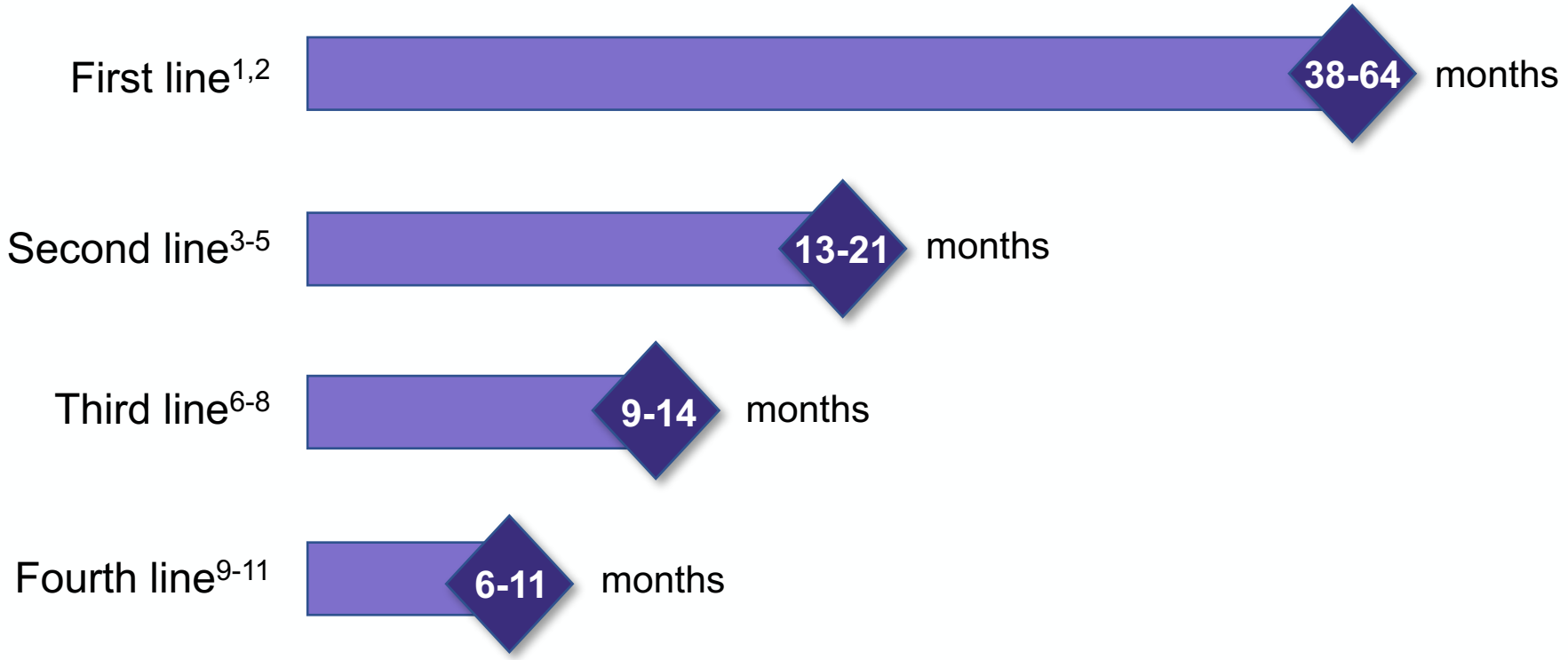
- Likely good response to initial therapy
- Eventual relapses to subsequent therapy

Therapeutic advances have improved disease control and long-term clinical outcomes[2-4]

- 10-year survival rate: 64% to 92%[2]
- Median survival is approximately 20 years, similar to age-matched controls[4-7]

1. ACS. Treating B-cell non-Hodgkin lymphoma. Follicular Lymphoma. https://www.cancer.org/cancer/non-hodgkin-lymphoma/treating/b-cell-lymphoma.html. Accessed 10/27/22. 2. Freedman A, Jacobsen E. *Am J Hematol*. 2020;95:316-327. 3. Kahl BS, Yang DT. *Blood*. 2016;127:2055-2063. 4. Provencio M et al. *PLoS ONE*. 2017;12:e0177204. 5. Maurer MJ et al. *Am J Hematol*. 2016;91:1096-1101. 6. Swenson WT et al. *J Clin Oncol*. 2005;23:5019-5026. 7. Tan D et al. *Blood*. 2013;122:981-987

Duration of Response With Successive Lines of Therapy



1. Czuczman MS, et al. *J Clin Oncol* 2004;22:4711-4716. **2.** Marcus R, et al. *J Clin Oncol* 2008;26:4579-4586. **3.** Johnson PWM, et al. *J Clin Oncol* 1995;13:140-147. **4.** Piro LD, et al. *Ann Oncol* 1999;10:655-661. **5.** Robinson KS, et al. *J Clin Oncol* 2008;26:4473-4479. **6.** Kahl BS, et al. *Cancer* 2010;116:106-114. **7.** Maloney DG, et al. *Blood* 1997;90:2188-2195. **8.** Witzig TE, et al. *J Clin Oncol* 2002;20:2453-2463. **9.** Davis TA, et al. *J Clin Oncol* 1999;17:1851-1857. **10.** Gopal AK, et al. *Blood* 2015;125:1236-1243. **11.** McLaughlin P, et al. *J Clin Oncol* 1998;16:2825-2833.

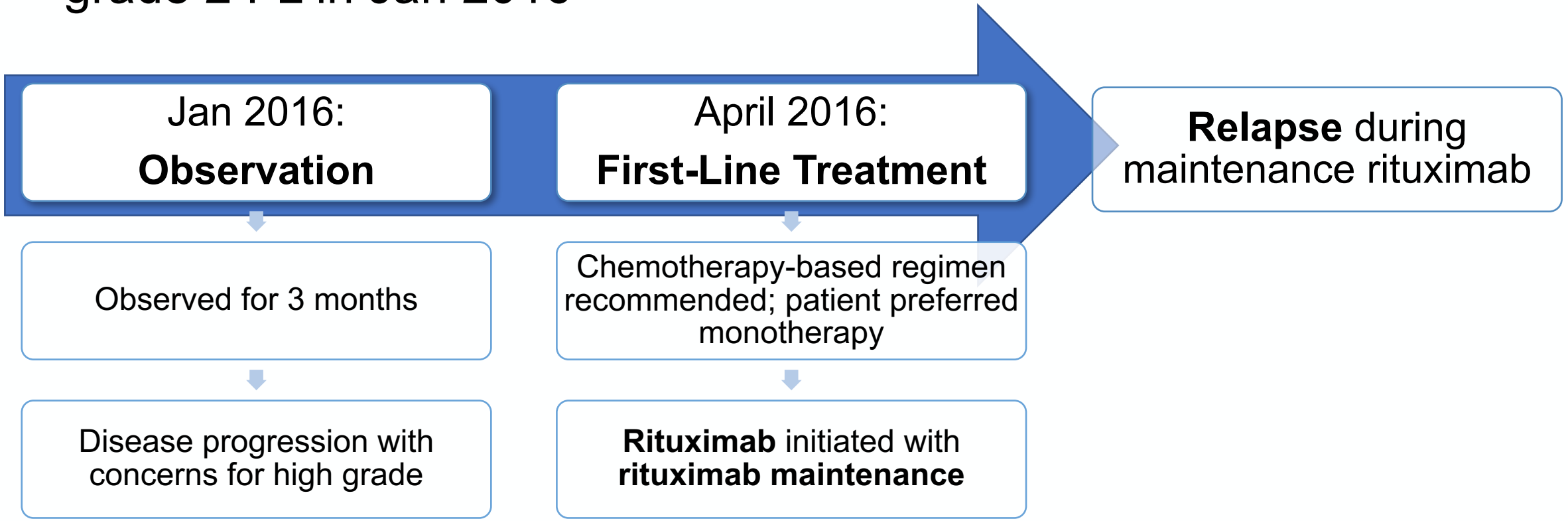
Current Treatment Options for Relapsed/Refractory FL

Second Line	≥Third Line
• Watch and wait • Chemoimmunotherapy (e.g., bendamustine + obinutuzumab, R-CHOP) • Lenalidomide + rituximab • Tazemetostat (only if not candidates for other alternatives) • Autologous stem cell transplant	• Any of the second-line options • Tazemetostat • CAR T-cell therapies

Case 2

Introduction to Case 2: Comorbidities

Mrs. Bryant is a 78-year-old woman who was diagnosed with grade 2 FL in Jan 2016



Case 2: Continued Therapy Despite Comorbidities

Nov 2016: Second-Line Treatment

- 6 cycles bendamustine + rituximab; achieved CR
- Completed 2 y rituximab maintenance

Late 2019: Comorbidities Develop

- Diagnosed with Crohn disease; treated with mesalamine: developed pancreatitis
- Admitted Dec 2019 for sepsis requiring intubation
- Heart failure identified with LVEF 25-30%
- Acute kidney injury

June 2020: Third-Line Treatment

- Lenalidomide + rituximab
- Developed rash from lenalidomide and Crohn disease flare; treated with prolonged course steroids

Oct 2021: Fourth-Line Treatment

- Cough and hilar mass; EBUS-guided biopsy identified grade 3a FL
- Initiated **tazemetostat (800 mg) BID**
- Mixed response, but stable disease; therapy continued

Treatment options are available for patients with FL who have complicated comorbidities

EBUS, endobronchial ultrasound; LVEF, left ventricular ejection fraction

Polling Question

What aspects of tazemetostat therapy are most important in your prescribing considerations?

A. Novel mechanism of action as compared to earlier lines of therapy **0%**

B. Safety profile of the medication **12%**

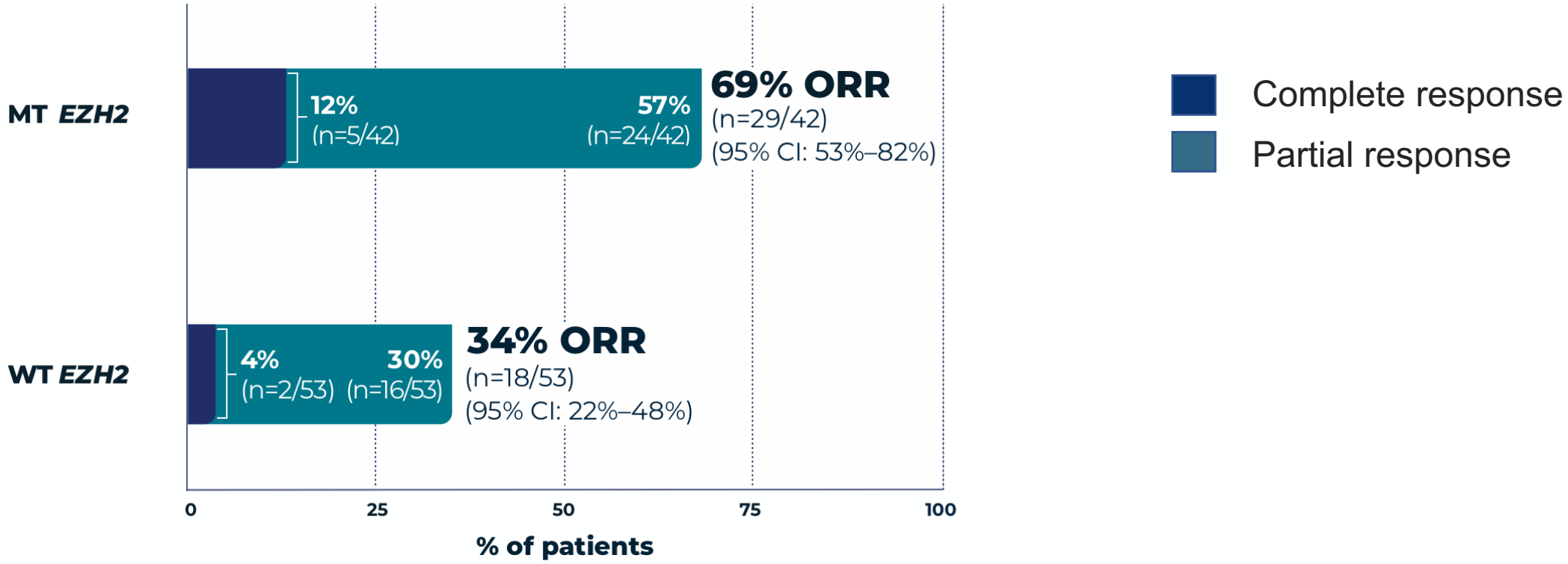
C. Time to response data **0%**

D. Ability to prescribe oral therapy as opposed to IV therapy **12%**

E. All of the above **75%**

Tazemetostat: Response Rates

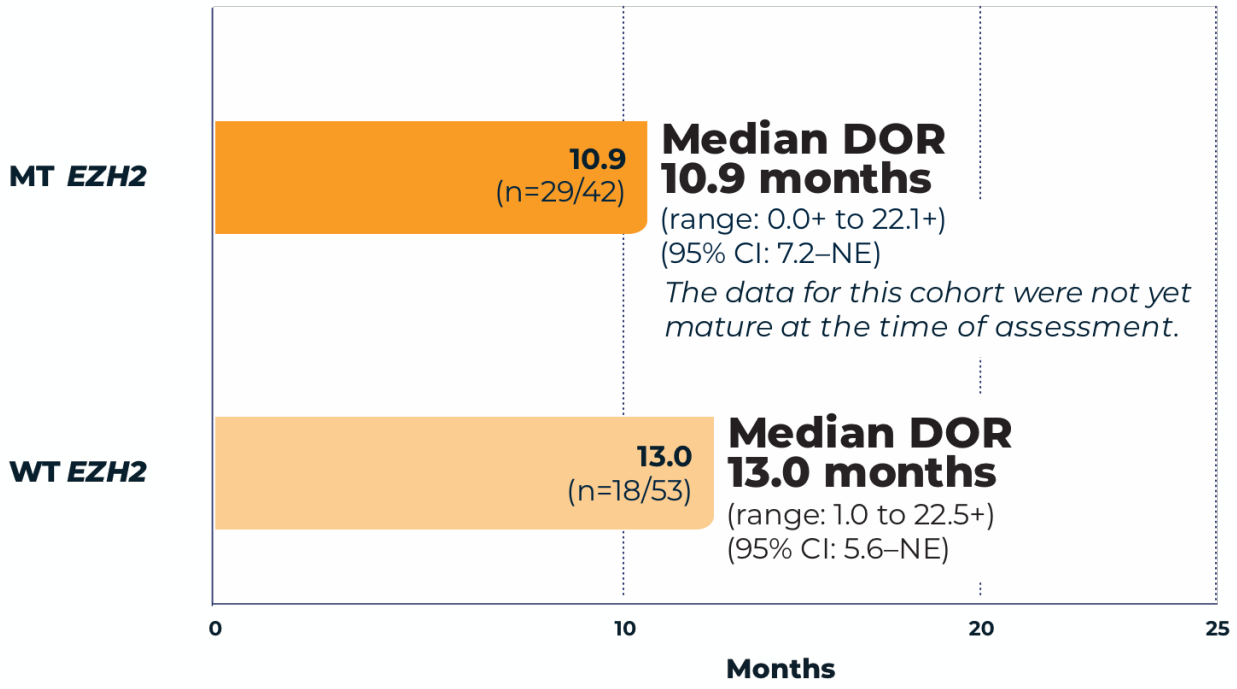
Tumor Response Rates to Tazemetostat in a Phase 2 Trial



Morschhauser F, et al. *Lancet Oncol*. 2020;21:1433–1442.

Tazemetostat: Duration and Time to Response

Median DOR to Tazemetostat in a Phase 2 Trial



DOR and Time to Response

	MT *EZH2*	WT *EZH2*
DOR		
≥6 months	59%	56%
≥12 months	21%	39%
Time to response, median	3.7 mo	3.9 mo

DOR, duration of response; MT, mutated; NE, not evaluable; WT, wild type

Morschhauser F, et al. *Lancet Oncol*. 2020; 21:1433–42.

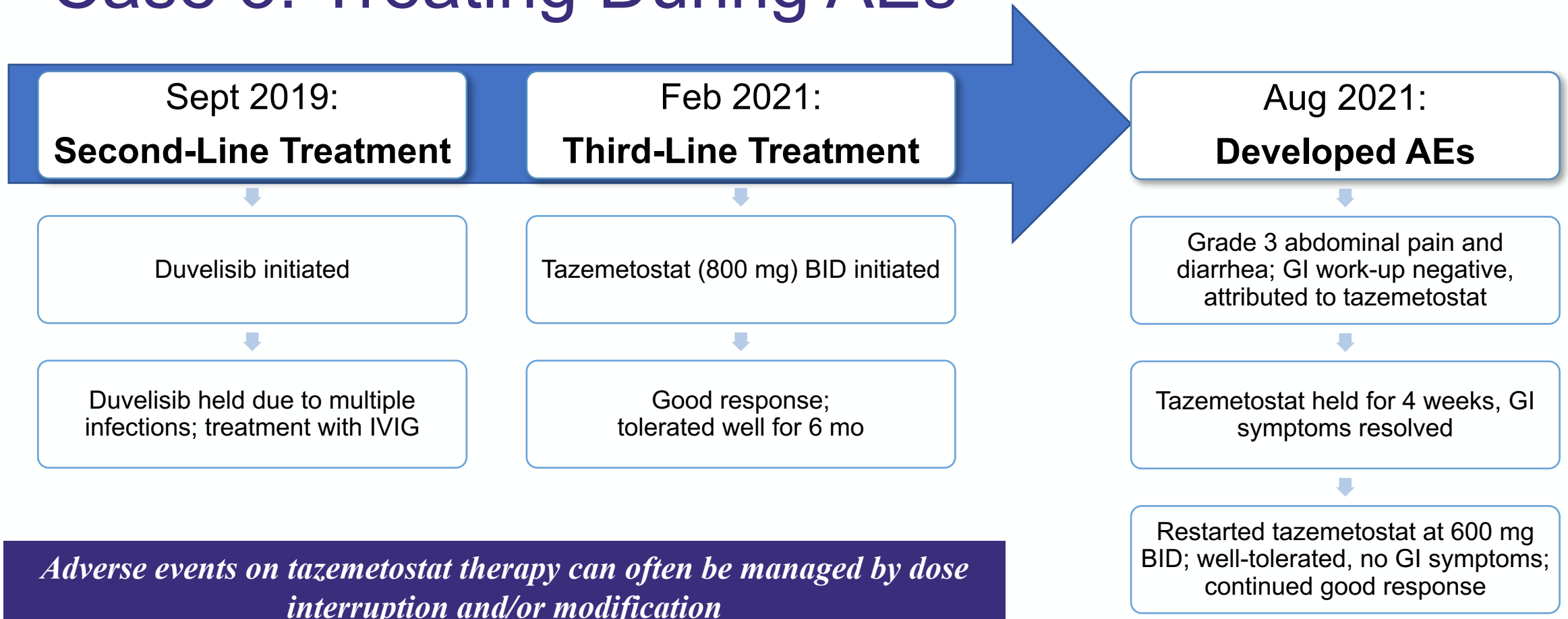
Case 3

Introduction to Case 3: Managing AEs

- Mr. Gordon is an 88-year-old man who was diagnosed with low-grade FL in Feb 2017
  - 70% bone marrow and osseous involvement
  - FLIPI 4; high risk
  - PMH: HTN, BPH, hypercholesterolemia, squamous cell cancer
- Treated with bendamustine + rituximab
- Completed maintenance rituximab Aug 2019

BPH, benign prostatic hyperplasia; FLIPI, Follicular Lymphoma International Prognostic Index; HTN, hypertension; PMH, past medical history

Case 3: Treating During AEs



Adverse events on tazemetostat therapy can often be managed by dose interruption and/or modification

IVIG, intravenous immune globulin

Favorable Safety Profile With Tazemetostat

- Hematologic grade 3-4 AEs were uncommon, affecting ≤4% of patients
  - 4% of patients developed serious TRAEs--thrombocytopenia
- TRAEs led to dose reduction in 9% and discontinuation in 5%
- No treatment-related deaths

Non-Hematologic TRAEs With Tazemetostat

AE	Grade 1-2	Grade 3-4
Nausea	19%	0
Diarrhea	12%	0
Alopecia	14%	0
Cough	2%	0
Asthenia	13%	1%
Fatigue	11%	1%
URTI	1%	0
Bronchitis	3%	0
Abdominal pain	2%	0
Headache	5%	0
Vomiting	6%	0
Pyrexia	2%	0

Morschhauser F, et al. *Lancet Oncol*. 2020; 21:1433–42.

Additional Considerations

- Avoid moderate-strong CYP3A inhibitors
  - If required, reduce tazemetostat dose
- Avoid moderate-strong CYP3A inducers

Drug-Drug Interactions

- High-fat meal does not significantly affect exposure
- Mild to severe renal impairment: no dose adjustment
- Mild hepatic impairment: no dose adjustment
  - Has not been studied in moderate to severe hepatic impairment

Dose Modifications

Tazverik (tazemetostat) tablets. [Prescribing information]. Cambridge, MA: Epizyme, Inc. 07/2020.

Polling Question

Administration of tazemetostat with strong or moderate CYP3A inhibitors may increase the frequency or severity of adverse reactions. Who in your clinic is most frequently responsible for medication reconciliation with oral oncolytics?

A. The NP or PA **0%**

B. The pharmacist **0%**

C. The oncologist **0%**

D. The NP, PA, or pharmacist **100%**

Key Takeaways

- Tazemetostat is an effective second-line or later therapy for patients with relapsed/refractory FL with an EZH2 mutation or who have limited treatment options.
- Tazemetostat may be safe to use for patients with comorbidities.
- Although potential adverse events can occur with tazemetostat, most are mild, and therapy can be continued with dose modifications.
- APs are an important part of the multidisciplinary team and can help guide treatment decisions and manage AEs.

Q & A

Please type your questions for Jennifer L. Garson
into the **question box** in the control panel.

Thank You