JADPRO Clinical Case Series

Considerations in Front-Line Treatment Selection for CLL

PRESENTER

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Objectives

- Understand the management of potential ibrutinib-associated adverse events (AEs)
- Discuss the role of advanced practitioners (APs) in the treatment of AEs
- Review case studies to understand AE treatment decision-making

Case 1

Introduction to Case 1: Diagnosed With CLL

- Mr. Garcia is a 68-year-old man incidentally diagnosed with asymptomatic CLL during active surveillance for prostate cancer
- Further testing identified an *IgVH* mutation, trisomy 12 by FISH, and no del(17p)
- Did not require treatment

Past Medical History


Hypertension

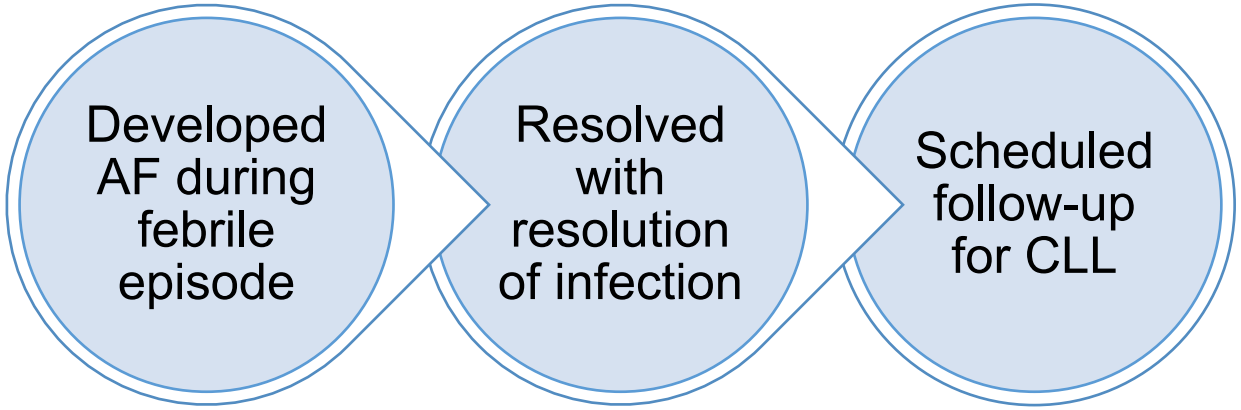

Obesity


OSA


CKD

Case 1: Develops Atrial Fibrillation

- Followed by active surveillance every 3 months for 2 years
- In February 2019, hospitalized for sepsis



Case 1: Treatment Selection

- Mr. Garcia has been experiencing increasing fatigue
- Ibrutinib + obinutuzumab was initiated
  - Only approved non-chemotherapy option in 2019

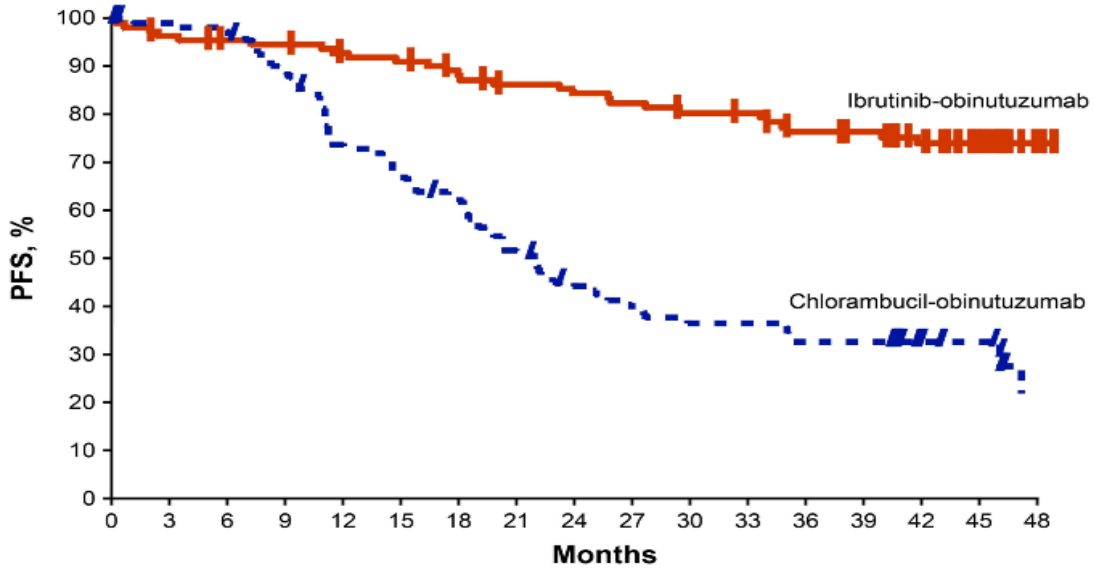
Laboratory Values

Parameters	Values
White blood cell count	75,000 cells/μL
Hemoglobin	10.1 g/dL
Platelets	188,000 cells/ μL
ALC	62,000 cells/μL

At diagnosis, ALC was 38,000 cells/μL

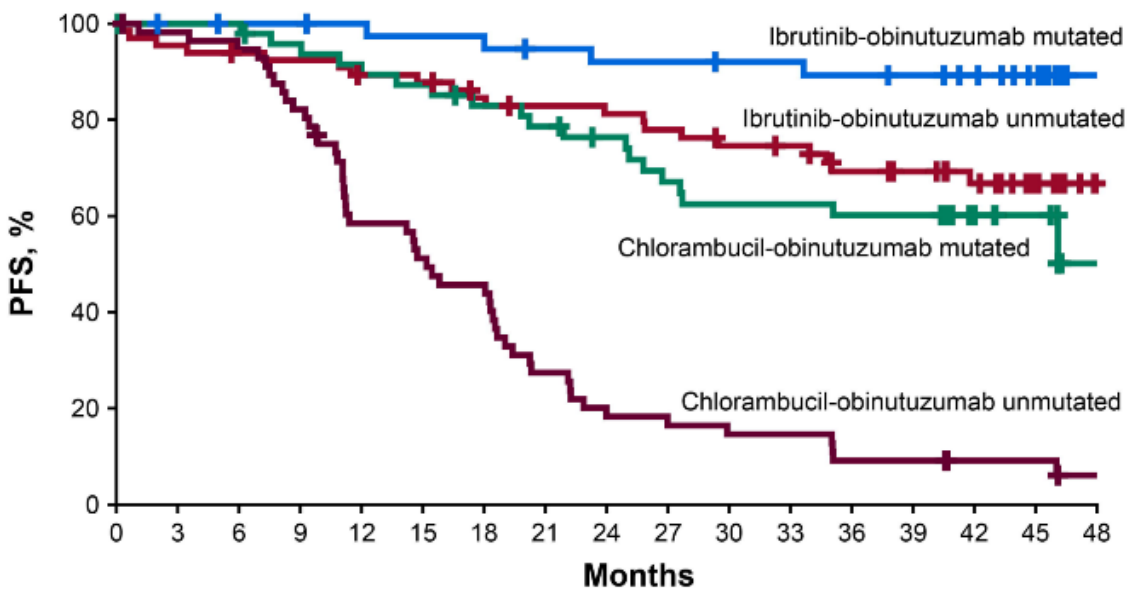
Phase 3 iLLUMINATE Trial

PFS in ITT Population



	Ibrutinib + obinutuzumab (mo)	Chlorambucil + obinutuzumab (mo)	HR (95% CI)
mPFS	NE	21.9	0.251 (0.162-0.389; p<.0001)

PFS Stratified by *IgVH* Mutation



	Ibrutinib + obinutuzumab (mo)	Chlorambucil + obinutuzumab (mo)	HR (95% CI)
mPFS, **unmutated**	49.0	15.2	0.17 (0.10-0.29; p<.0001)
mPFS, **mutated**	NE	NE	0.20 (0.07-0.59; p=.001)

Moreno C et al. *Haematologica*. Published online Jan 13, 2022.

Case 1: Develops AE

- After second cycle, bilateral lower extremity (BLE) edema developed
- Ultrasound showed no DVT or enlarged inguinal lymph nodes
- Echocardiogram showed normal EF
- Determined likely to be due to ibrutinib
  - Treated with furosemide

BLE Edema Differential

- LV dysfunction
- Lymphedema
- DVT
- Ibrutinib

Case 1: Response to Treatment

- 5 years: Continues to take ibrutinib with excellent response
  - No other complications
  - No AF recurrence
- Follow-up with AP continues every 3-4 months

Polling Question

How often do you see patients on long-term ibrutinib (>2 years) for follow-up?

A. Every month **14%**

B. Every 3 to 4 months **55%**

C. Every 6 months **27%**

D. Every year **5%**

Case 2

Introduction to Case 2: Diagnosis

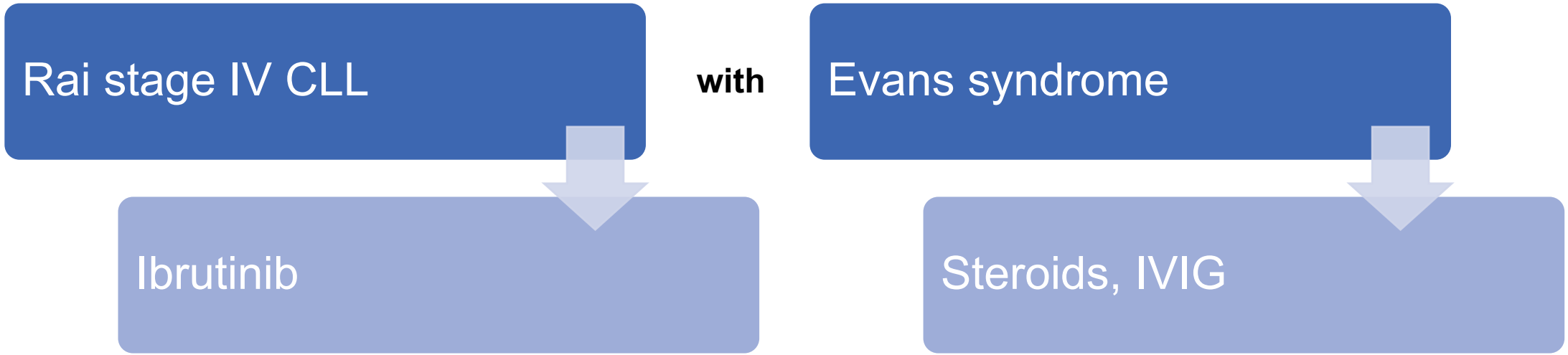
- Ms. Anderson is a 48-year-old woman
- Presented to ED with flu-like symptoms, several nosebleeds, bleeding gums, blood blisters in mouth
- Urgently admitted with anemia, positive direct Coombs test, indirect hyperbilirubinemia, decrease haptoglobin, elevated LDH

Laboratory Values

Parameters	Values
White blood cell count	79,000 cells/μL
Hemoglobin	9.2 g/dL
Platelets	2,000 cells/ μL
Bone marrow biopsy	70% CLL involvement, adequate megakaryocytes
FISH	Del(13q)
Hypermutation analysis	*IgVH* unmutated

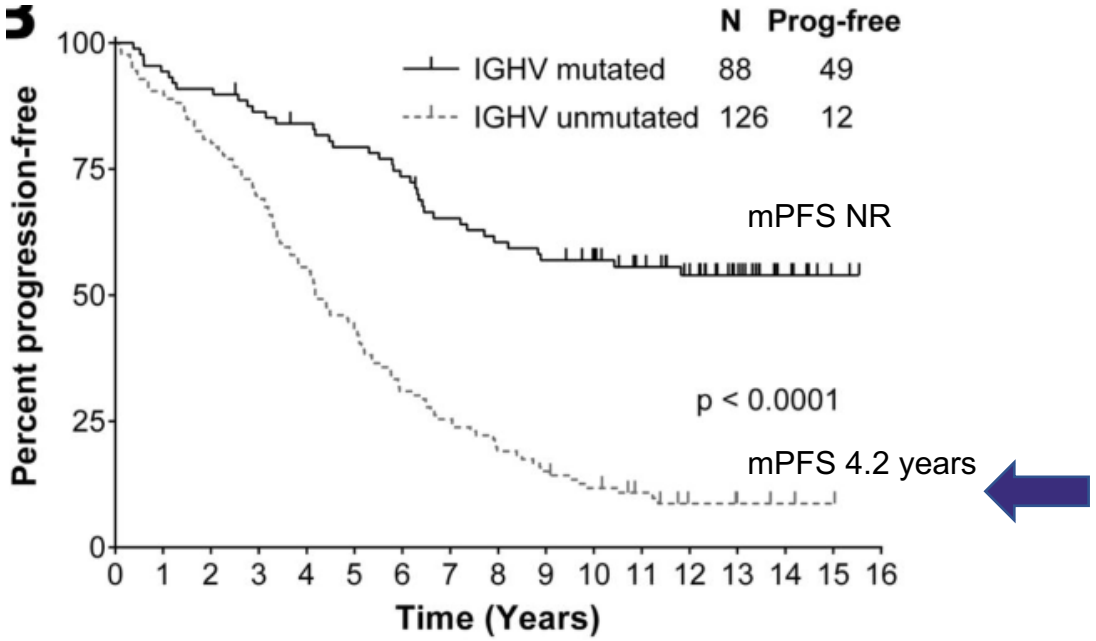
Case 2: Treatment Complicated by Evans Syndrome

- Diagnosed with:



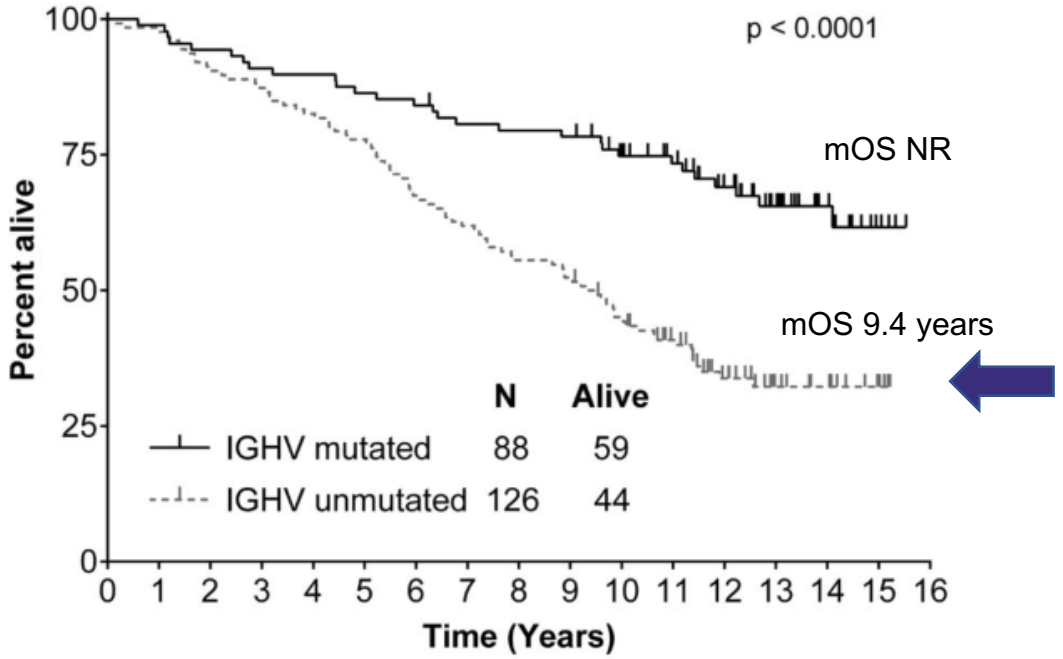
Unmutated *IgVH*: Inferior Outcomes With Chemoimmunotherapy

PFS Stratified by IgHV Status



HR, 3.62 (95% CI, 2.50-5.24; p<.001)

OS Stratified by IgHV Status



HR, 2.62 (95% CI, 1.71-4.01; p<.001)

Thompson PA et al. *Blood*. 2016;127:303-309.

Case 2: Treatment Response

CLL

- After 1 month, decrease in ALC

Evans syndrome

- Platelets remained low after 2 courses pulse steroids and IVIG
- Started IV rituximab
- After third cycle of rituximab, neutropenia developed (treated to resolution with G-CSF)
- No additional doses of rituximab given

Case 2: Long-Term Ibrutinib

- Within 1 year after starting ibrutinib, Ms. Anderson achieved a CR by peripheral blood cytometry and bone marrow biopsy
- At 5-year follow-up, Ms. Anderson remained in remission
  - Asked about obinutuzumab + venetoclax
  - Fixed-duration ibrutinib?

Laboratory Values

Parameters	Values
WBC	3,800 cells/μL
ANC	2,350 cells/μL
ALC	1,160 cells/μL
Hemoglobin	12.3 g/dL
Platelets	93,000 cells/ μL

Polling Question

How do you counsel patients with CLL who ask how long they'll need to continue therapy with ibrutinib?

A. It's OK to stop ibrutinib as soon as there is complete remission of CLL and restart again when there is disease progression **13%**

B. At this time, ibrutinib is recommended indefinitely for the best response **53%**

C. If there is complete remission of CLL, you can stop therapy after 5 years **20%**

D. If there is MRD negativity, you can stop therapy after 5 years **13%**

Case 3

Introduction to Case 3: Diagnosis

- Mr. Thompson was 55 years old when he was diagnosed with Rai stage 0 CLL, del(13q)
- Active surveillance every 3 to 6 months for 3 years
- At 3-year visit, reported fatigue, nausea, and bloating
  - Left axillary, bilateral supraclavicular, B cervical, mesenteric, periportal, and pelvic lymph node involvement
    - Most 2-3 cm, largest 2.4 x 4.5 cm and SUV 5-6
    - No transformation

Laboratory Values

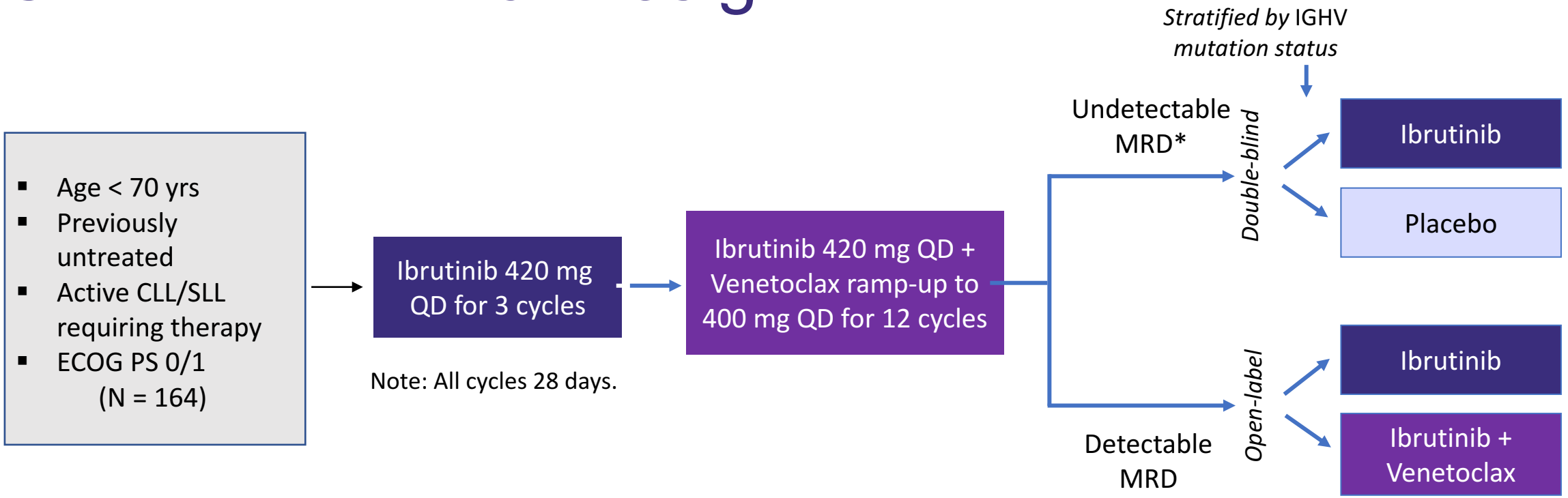
Parameters	Initial	3 Years
WBC	15,000 cells/µL	30,400 cells/µL
ALC	11,000 cells/µL	22,900 cells/µL
Hemoglobin	14 g/dL	
Platelets	340,000 cells/ µL	

LDH 250 U/L

Case 3: Treatment

- Options discussed
  - Ibrutinib
  - Obinutuzumab + venetoclax
  - Clinical trial
- Opted to enroll in phase II CAPTIVATE trial

CAPTIVATE Trial Design



- **Primary endpoint:** 1-year DFS in patients with confirmed, undetectable MRD
- **Secondary endpoints:** undetectable MRD rates, response, PFS, safety

*Defined as having undetectable MRD (< 10^{-4} by flow cytometry) serially over at least 3 cycles in both PB and BM

Wierda WG et al. *J Clin Oncol*. 2021;39:3853-3865.

Case 3: Treatment Assignment

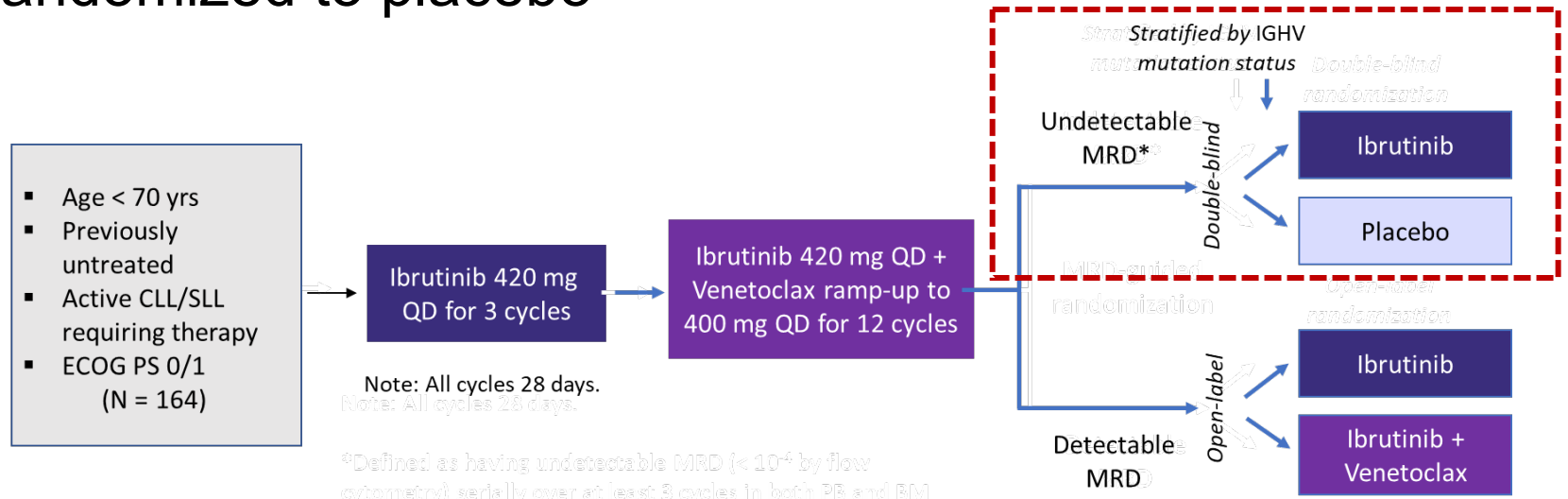
- Randomly assigned to fixed-duration arm
  - Received 3 cycles of ibrutinib followed by ibrutinib + venetoclax for 12 cycles
- 3 months after starting therapy, developed fingernail pain and loss of curly hair
  - Referred to dermatology
  - Attributed to ibrutinib
  - Diagnosed with paronychia/excess granulation tissue and treated with clobetasol ointment, warm soaks, mupirocin ointment

Case 3: QOL Considerations

- Developed erythematous maculopapular rash on chest, treated to resolution with topical steroids
- Primary complaints of ibrutinib + venetoclax treatment:
  - Fatigue
  - Intermittent rash
  - Pain due to paronychia and onychorrhexis
  - Curly hair became straight
  - Mild fatigue

Case 3: Treatment Response

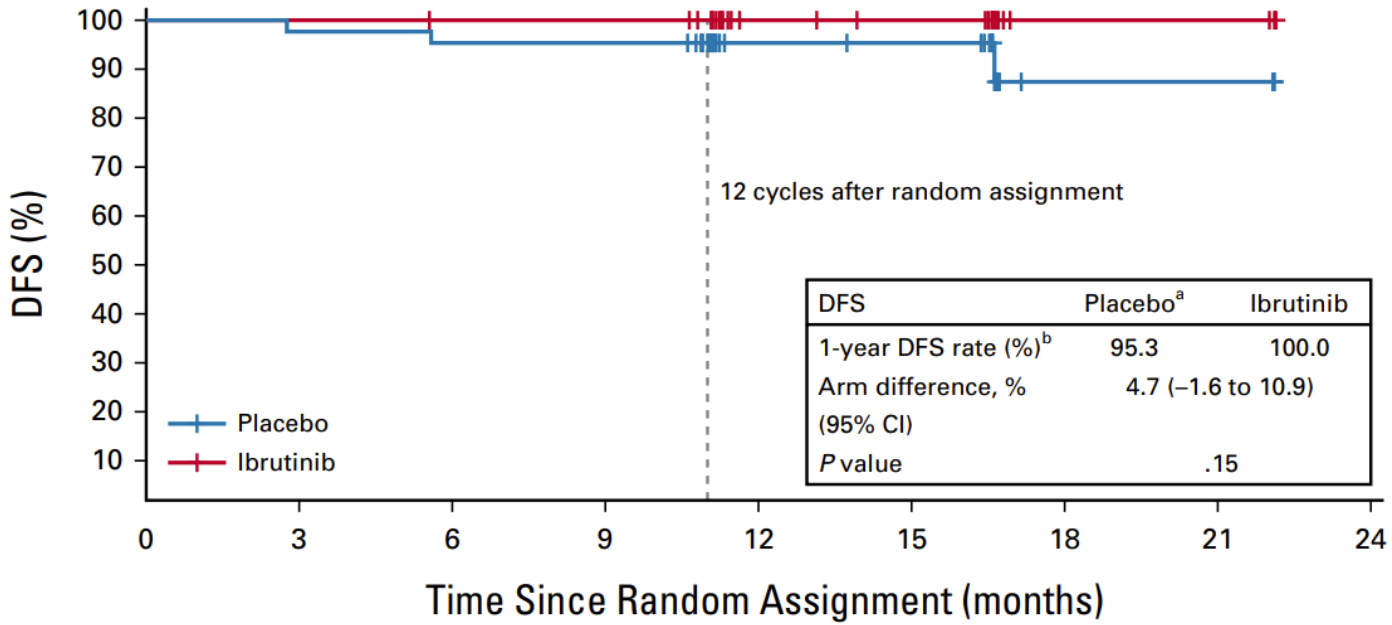
- At end of treatment, no MRD as assessed by 8-color flow cytometry
  - Randomized to placebo



CAPTIVATE Results

- Fixed-duration treatment may be possible for patients with confirmed undetectable MRD

Similar 1-Year PFS Between Placebo and Ibrutinib After Random Assignment



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Polling Question

How often do you present clinical trials as a potential treatment option for patients requiring first-line therapy?

A. Frequently. We have several clinical trials at my institution, and I am well versed in the research landscape. **0%**

B. Sometimes. We have several clinical trials at my institution, but I have a hard time keeping up with the available options. **38%**

C. Rarely. We do not have clinical trials at my institution, so I would need to refer. **15%**

D. Never. I leave this decision up to the oncologist. **46%**

Q & A

Please type your questions for Laura
into the **question box** in the control panel.

Thank You