APTITUDE HEALTH®

CASES

INSIGHTS INTO ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

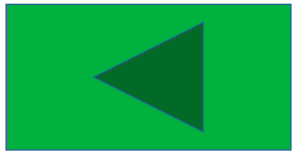
Thursday, March 11, 2021

Community Insights From Central Region

HOW TO NAVIGATE THIS REPORT

CASES

Click to move to topic of interest or ARS supporting data



Click to return to previous slide

CONTENTS

CASES

REPORT OBJECTIVES

CASES

STUDY OBJECTIVES

- To gain advisors' perspectives on current treatment practices and management of adult and adolescent and young adult (AYA) acute lymphoblastic leukemia (ALL) patients

REPORT SNAPSHOT: SESSION OVERVIEW

CASES

A moderated roundtable discussion was held with community oncologists from the central region of the United States in a virtual setting on **March 11, 2021**

Disease state and data presentations were led by **Dr Elias Jabbour** from MD Anderson Cancer Center in conjunction with content developed by the Aptitude Health clinical team

Insights on current treatment practices regarding adult and AYA ALL patients, including assessment and monitoring of MRD in the community setting, were obtained

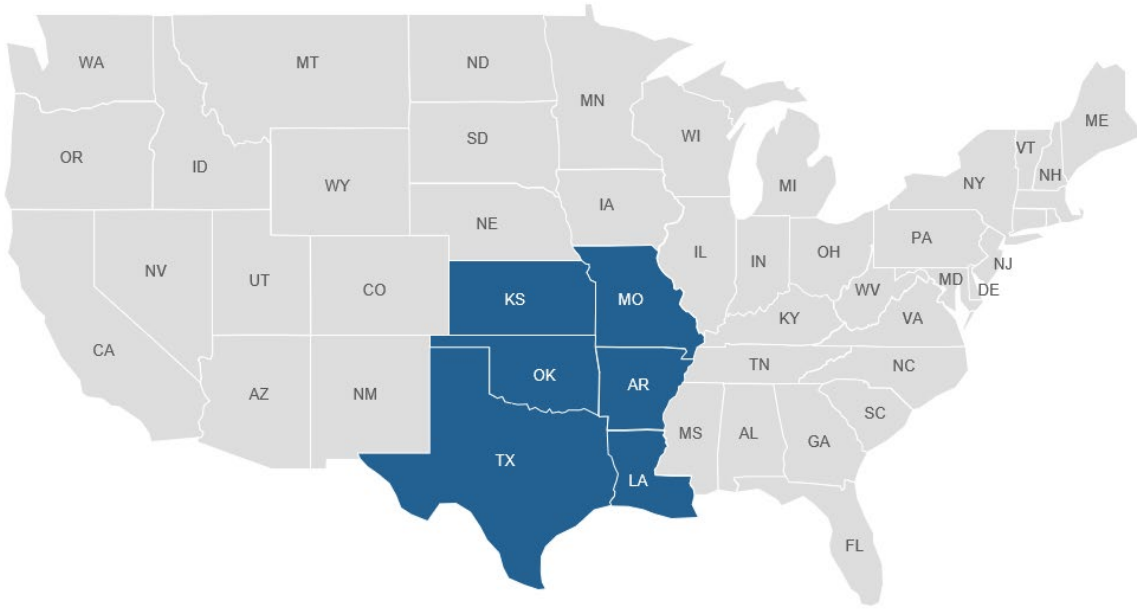
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

REPORT SNAPSHOT: ATTENDEE OVERVIEW

CASES

- The group of advisors comprised 8 community oncologists from the central United States
  - Attendees of the roundtable represented community oncologists from Texas, Missouri, and Kansas

INSTITUTION	CITY	STATE
University of Texas Health Center	Abilene	TX
St Louis University	St Louis	MO
The Center for Cancer and Blood Disorders	Fort Worth	TX
Texas Oncology	Dallas	TX
Cancer Care Kansas	Wichita	KS



REPORT SNAPSHOT: AGENDA

CASES

Time (CST)	Topic
6.00 PM – 6.15 PM (15 MIN)	**Introduction** • Program overview • Baseline ARS questions
6.15 PM – 7.25 PM (70 MIN)	**ALL – Management of First-Line Therapy** • Overview of current data – Impact of risk-stratification, age, and biomarkers on treatment (adult vs AYA, Ph+ vs Ph– vs Ph-like) – Differentiation of TKIs for Ph+ patients – Use of hyper-CVAD vs multiagent chemotherapy – Defining the appropriate patient for pediatric-inspired regimens – Response assessment and MRD monitoring – Management of MRD+ disease – Inclusion of monoclonal antibodies into therapy (inotuzumab ozogamicin, blinatumomab) • Reaction and discussion
7.25 PM – 7.35 PM (10 MIN)	**BREAK**
7.35 PM – 8.45 PM (70 MIN)	**ALL – Management of Relapsed Disease** • ARS questions • Overview of current data – Duration of response, impact of reinduction, and patient selection for transplant – Inclusion of monoclonal antibodies into therapy (inotuzumab ozogamicin, blinatumomab) – CAR T therapy • Reaction and discussion
8.45 PM – 9.00 PM (15 MIN)	**Key Takeaways and Meeting Evaluation**

APTITUDE HEALTH®

CASES

Topline Takeaways

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS

CASES

OBJECTIVE	PROCESS	INSIGHTS
• Understand physicians' expectations for clinical trial data before trying a new regimen in frontline for DLBCL • Gain insights into R/R patient referral patterns between academic and community practices • Assess the perception of polatuzumab in the R/R setting compared with other therapeutics (especially CAR T therapy and tafasitamab), including therapy selection and sequencing	Through AIRS questions and moderated discussions, community oncologists described their testing practices and challenges they experience	• Advisors are open to trying new regimens, primarily with good OS benefit data in frontline, with some open to adopting new therapy with good hazard ratio (0.80 or better) or EFS • Advisors in community practice typically treat older, less mobile, transplant-ineligible patients and refer out young, fit, transplant-eligible patients • All advisors generally have positive opinions/experiences with polatuzumab in terms of efficacy and tolerability; however, some currently use it only as a bridge to CAR T, and some in patients ineligible for CAR T. All advisors are unsure about sequencing therapies

APTITUDE HEALTH®

CASES

Key Insights and Discussion Summary

KEY INSIGHTS: MANAGEMENT OF FIRST-LINE THERAPY

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 1 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS: MANAGEMENT OF FIRST-LINE THERAPY

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS: MANAGEMENT OF FIRST-LINE THERAPY

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS: MANAGEMENT OF FIRST-LINE THERAPY

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 1 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

DISCUSSION: MANAGEMENT OF FIRST-LINE THERAPY

CASES

INSIGHTS

"Pathology does our bone marrows and we do send it out for NGS"

- Treatment success in frontline DLBCL

"We overall survival, that's what we need. This is not metastatic disease, this is curable disease, so we need overall survival."

"...cure without any significant long-term toxicity. ...I think when I define success, I would rather use a landmark endpoint rather than using OS or PFS, and I would say what's the disease free rate at 2 years. I definitely do think OS is important if there is significant toxicity with the treatment, and people dying from competing comorbidities..."

- Data needed to switch from SOC in frontline

"First of all, a lot of things have been tried, nothing is better than R-CHOP, and frankly, I'm pretty happy with how R-CHOP performs for my patients."

"I would be a late adopter. I would not be one of the first ones to move based on PFS or anything like that. I want something that's tried and true and we know how well it works."

"If the toxicities are not very severe, I think a hazard ratio of 0.85 or better would be something that I would be looking at."

"Overall survival data, that's ideal, but in this disease state OS is hard to come by, so you do have to use some surrogates of efficacy. So, I do think that a 2- or 3-year event-free survival kind of story is likely what's going to start driving my use of any regimen. ...PFS is NOT sufficient."

KEY INSIGHTS: MANAGEMENT OF RELAPSED DISEASE

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 1 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS: MANAGEMENT OF RELAPSED DISEASE

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 1 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

KEY INSIGHTS: MANAGEMENT OF RELAPSED DISEASE

CASES

How and when is MRD assessed by community oncologists and does it impact use of blinatumomab in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital.
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment.
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most advisors.
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation.
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments.

DISCUSSION: MANAGEMENT OF RELAPSED DISEASE

CASES

INSIGHTS

". . . In general, if a patient relapses, I generally refer those guys to an academic center . . ."

- Treatment success in frontline DLBCL

- Data needed to switch from SOC in frontline

APTITUDE HEALTH®

CASES

Advisor Key Takeaways

ADVISOR KEY TAKEAWAYS (1/2)

CASES

ADVISOR		ADVISOR	
1	> MRD, MRD, MRD!	6	> Importance of checking MRD status frequently > In young population, the use of hyper-CVAD vs more pediatric-
2	[illegible]	7	[illegible]
3	[illegible]	8	[illegible]
4	[illegible]	9	[illegible]

ADVISOR KEY TAKEAWAYS (2/2)

ADVISOR		ADVISOR	
	> For the TKI patients, seeing the success rates that we're		
1	[illegible]	5	[illegible]
2	[illegible]	6	[illegible]
3	[illegible]	7	[illegible]
4	[illegible]	8	[illegible]

APTITUDE HEALTH®

CASES

ARS Data – Introductory ARS Questions

MOST ADVISORS SEE 3–10 ALL PATIENTS PER YEAR (N = 8)

How many new ALL patients do you see per year?

BLINATUMOMAB HAS BEEN USED IN 1–3 UNIQUE ALL PATIENTS BY MOST EXPERTS (N = 8)

In how many unique ALL patients have you ever used blinatumomab (Blincyto)?

INOTUZUMAB OZOGAMICIN HAS BEEN USED IN 1–3 UNIQUE ALL PATIENTS BY MORE THAN HALF OF THE ADVISORS (N = 8)

CASES

In how many unique ALL patients have you ever used inotuzumab ozogamicin (Besponsa)?

APTITUDE HEALTH®

CASES

ARS Data – Management of First-Line Therapy

HYPER-CVAD + TKI IS THE PREFERRED INDUCTION REGIMEN FOR ADULT Ph+ ALL PATIENTS (N = 8)

CASES

My preferred induction regimen for adult Ph+ ALL patients is:

HYPER-CVAD + RITUXIMAB IS THE PREFERRED INDUCTION REGIMEN FOR ADULT Ph– ALL PATIENTS (N = 8)

CASES

My preferred induction regimen for adult Ph– ALL patients is:

MOLECULAR PCR AND NGS PLATFORM ARE THE MOST USED METHODS TO ASSESS MRD (N = 8)

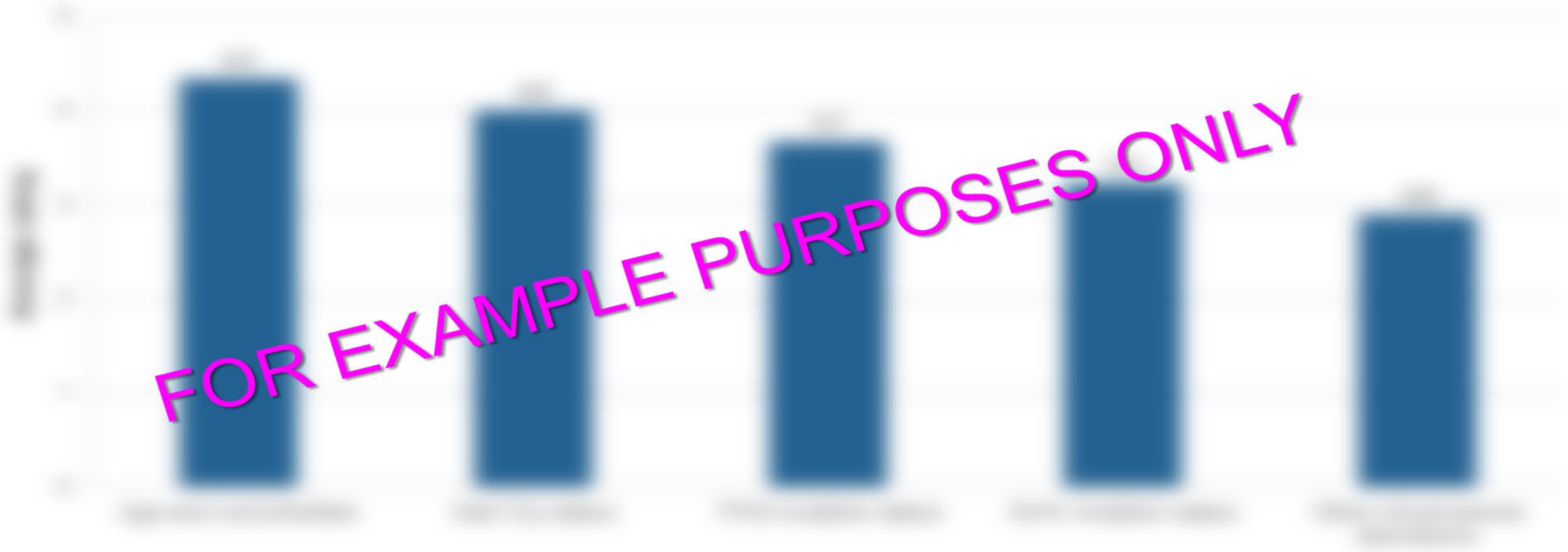
CASES

How do you assess for minimal residual disease (MRD)?

MRD IS ASSESSED AT CR BY HALF THE ADVISORS. THE OTHER EXPERTS ASSESS MRD MAINLY AT CR AND 3 MONTHS FROM INDUCTION, AND EVERY 3 MONTHS THEREAFTER (N = 8)

CASES

When do you assess for MRD?

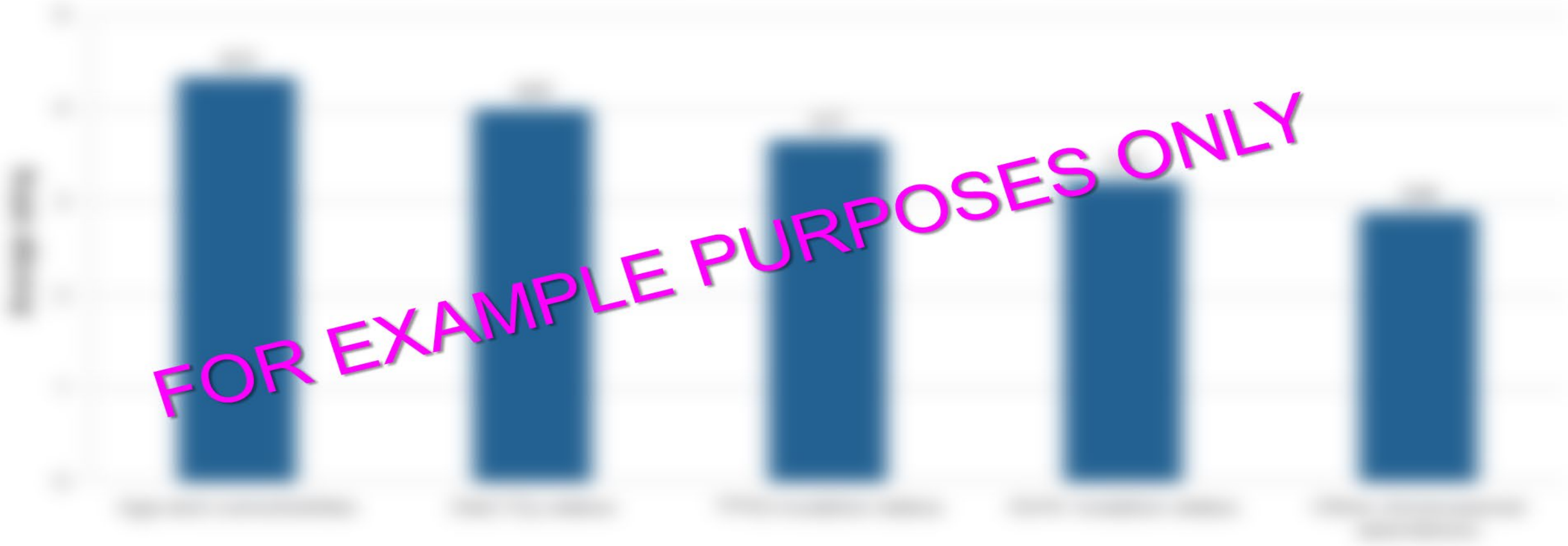


and every 3 months thereafter

THE ADVISORS CONSIDER BLINATUMOMAB INDUCING A RESPONSE RATE OF 80% IN MRD POSITIVE PATIENTS, WITH RESPONDING PATIENTS SHOWING OS AND PFS IMPROVEMENT (N = 8)

CASES

In patients with positive MRD treated with blinatumomab (select all that apply):



AYA ALL PATIENTS ARE DEFINED AS 15–39 YEARS OLD BY MOST ADVISORS (N = 8)

How do you define AYA ALL?

AYA PATIENTS ARE MAINLY TREATED WITH PEDIATRIC-INSPIRED REGIMENS (N = 8)

CASES

In general, how do you treat AYA patients?

PATIENT CASE

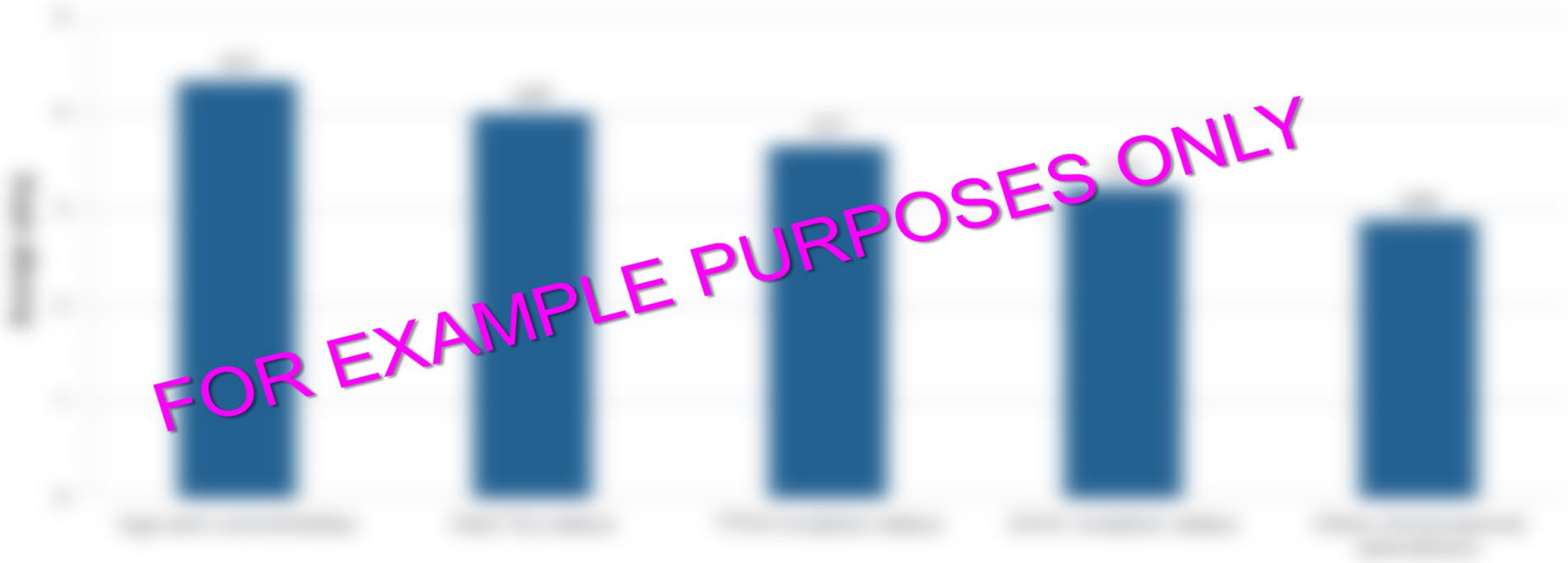
CASES

- Twenty-four-year-old female patient with no PMH presents with fatigue and easy

HALF THE ADVISORS WOULD TREAT THE DESCRIBED PATIENT WITHIN CLINICAL TRIALS, WHILE LESS THAN HALF WOULD USE A PEDIATRIC-INSPIRED INDUCTION REGIMEN (N = 8)

CASES

How would you treat her?



PATIENT CASE (CONTINUED)

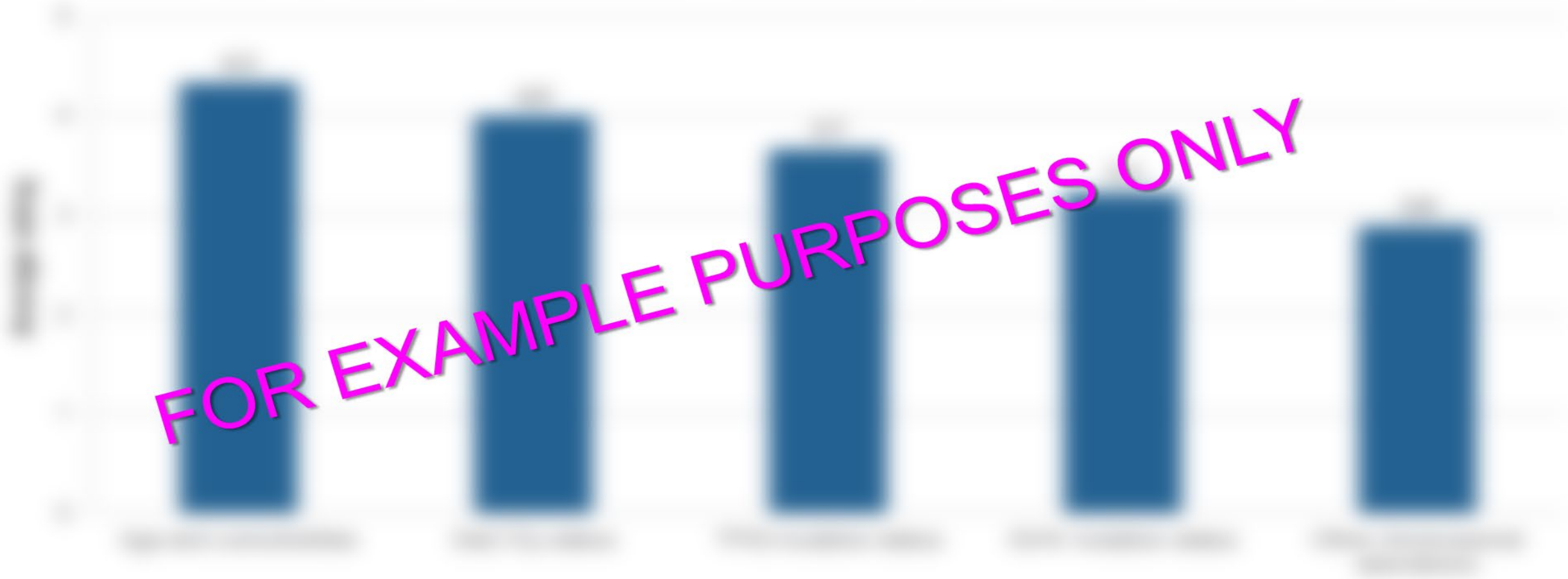
CASES

- Day 28 bone marrow assessment confirms CR. MRD is detected by flow

BLINATUMOMAB WAS RECOMMENDED AS THE NEXT TREATMENT BY MORE THAN HALF THE ADVISORS WHEN THE PATIENT IS MRD-POSITIVE AT CR (N = 7*)

CASES

What do you recommend next?



*One advisor did not respond.

PATIENT CASE (CONTINUED)

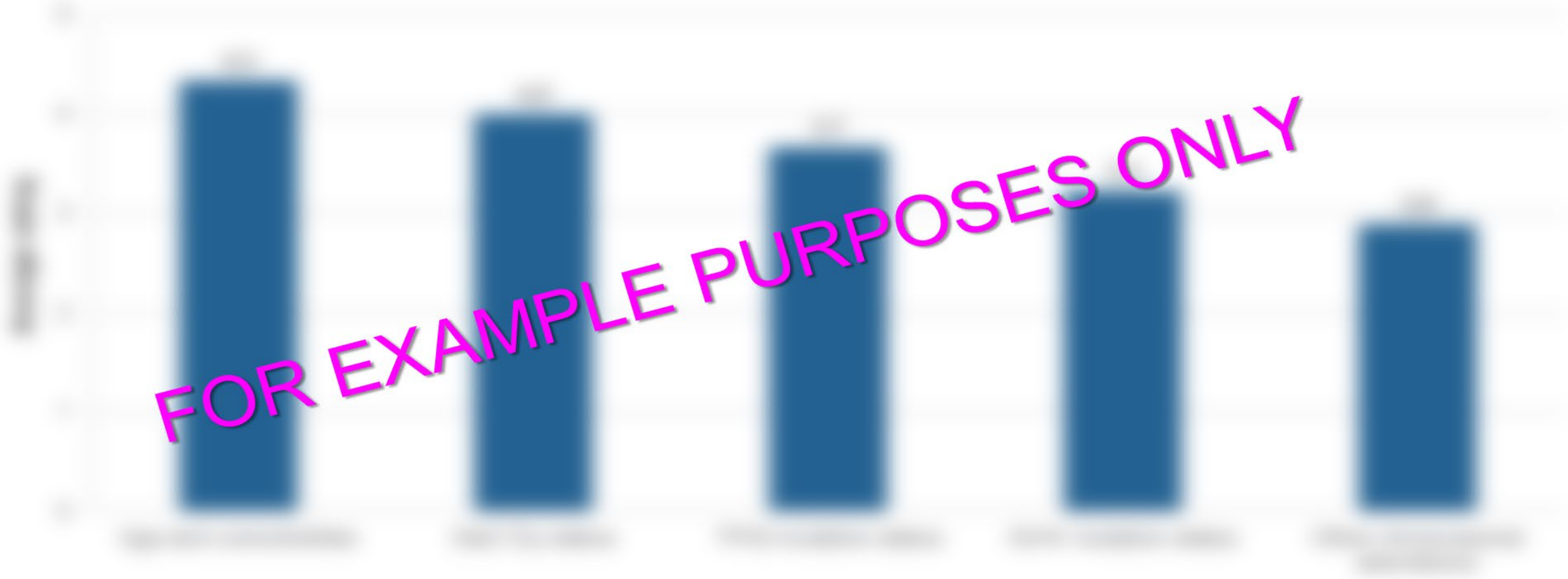
CASES

- The patient received further consolidation therapy. MRD assessment at 12 weeks

BLINATUMOMAB ± SCT WOULD BE USED BY HALF THE ADVISORS IN PATIENTS WITH 0.01% ABERRANT BLASTS AFTER FURTHER CONSOLIDATION THERAPY (N = 8)

CASES

What do you recommend next?



APTITUDE HEALTH®

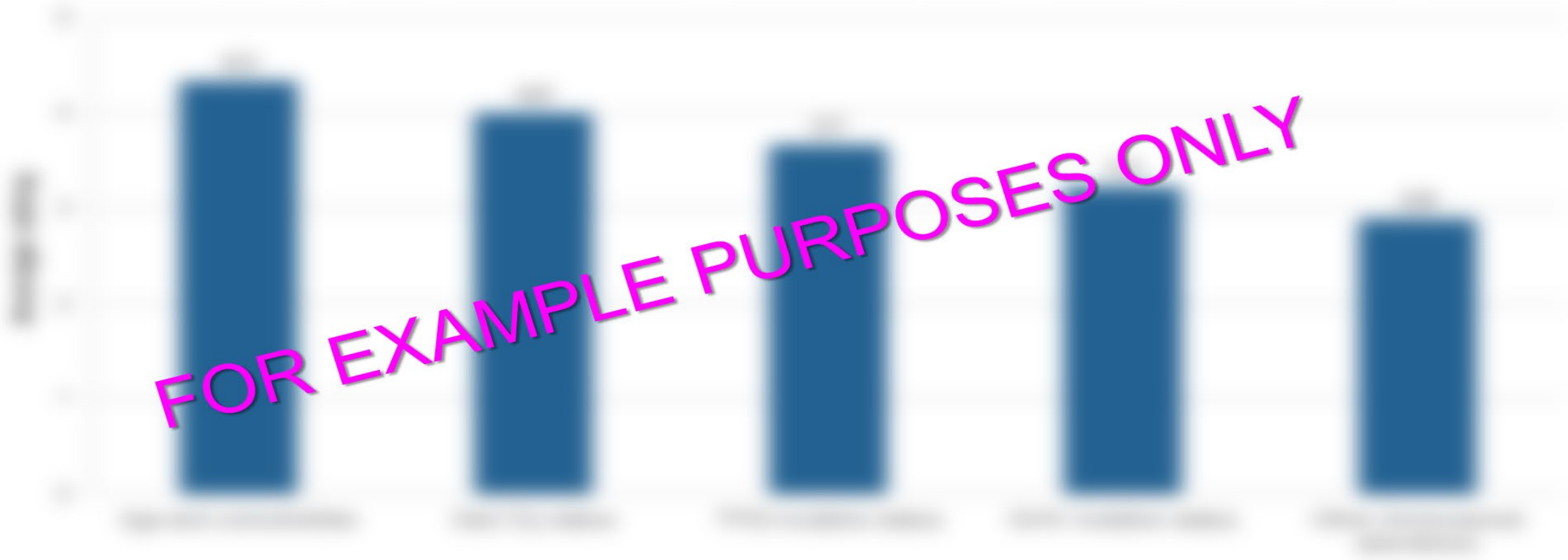
CASES

ARS Data – Management of Relapsed Disease

FOR MOST ADVISORS, INOTUZUMAB OZOGAMICIN IMPROVES MRD-NEGATIVITY RATE, RESPONSE RATE AND DURATION OF RESPONSE IN R/R ALL PATIENTS (N = 7*)

CASES

When compared with SOC in patients with relapsed/refractory ALL, inotuzumab ozogamicin (select all that apply):

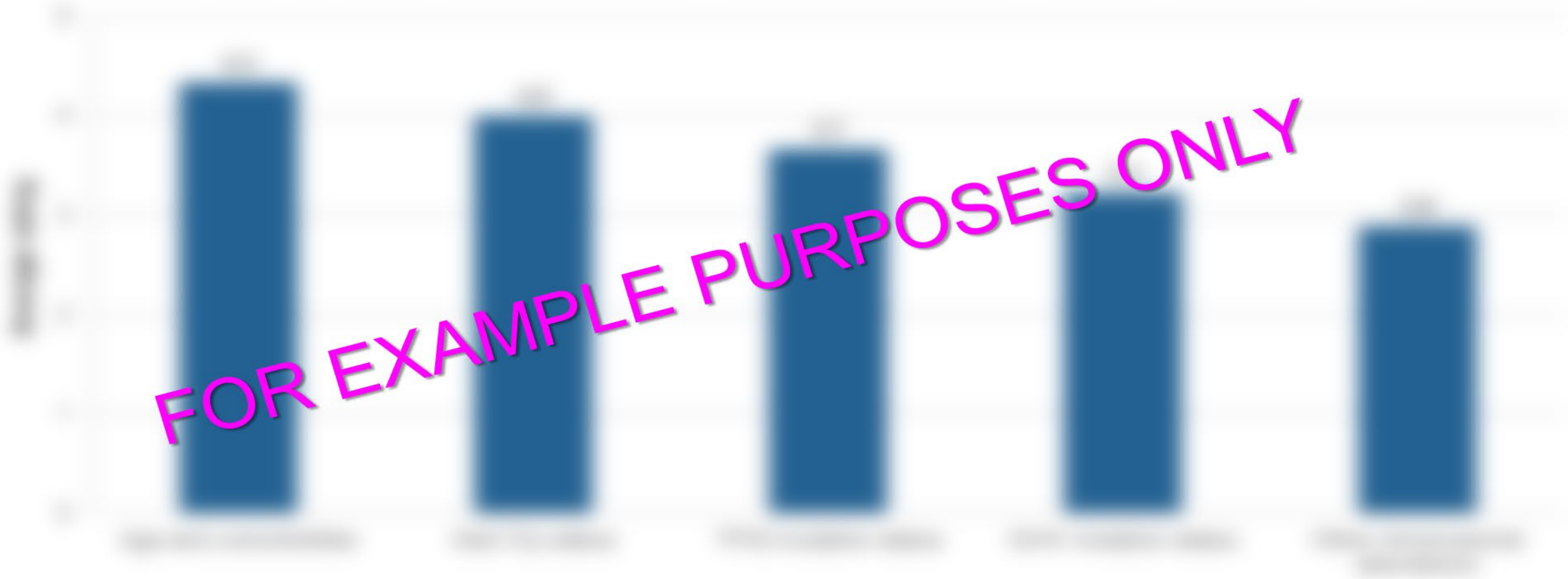


*One advisor did not respond.

FOR NEARLY ALL ADVISORS, BLINATUMOMAB IMPROVES OS IN R/R ALL PATIENTS (N = 6*)

CASES

When compared with SOC in patients with relapsed/refractory ALL, blinatumomab improves OS.



*Two advisors did not respond.

PATIENT CASE

CASES

- Forty-five-year-old male presents with fever and fatigue. CBC reveals: Hgb = 9

RITUXIMAB–HYPER-CVAD IS THE PREFERRED INDUCTION THERAPY FOR THE DESCRIBED PATIENT SCENARIO (N = 7*)

CASES

What is your plan for induction therapy?

*One advisor did not respond.

PATIENT CASE (CONTINUED)

CASES

- The patient was treated with R–hyper-CVAD and achieved a CR with MRD

BLINATUMOMAB IS THE PREFERRED SALVAGE APPROACH FOR THE DESCRIBED PATIENT SCENARIO (N = 7*)

CASES

What would be your salvage approach?

*One advisor did not respond.

PATIENT CASE (CONTINUED)

CASES

- The patient received reinduction with augmented hyper-CVAD. On day 28 he

STEM-CELL TRANSPLANT IS RECOMMENDED IF A DONOR IS AVAILABLE FOR THE DESCRIBED PATIENT SCENARIO (N = 8)

CASES

What would you now recommend?

PATIENT CASE (CONTINUED)

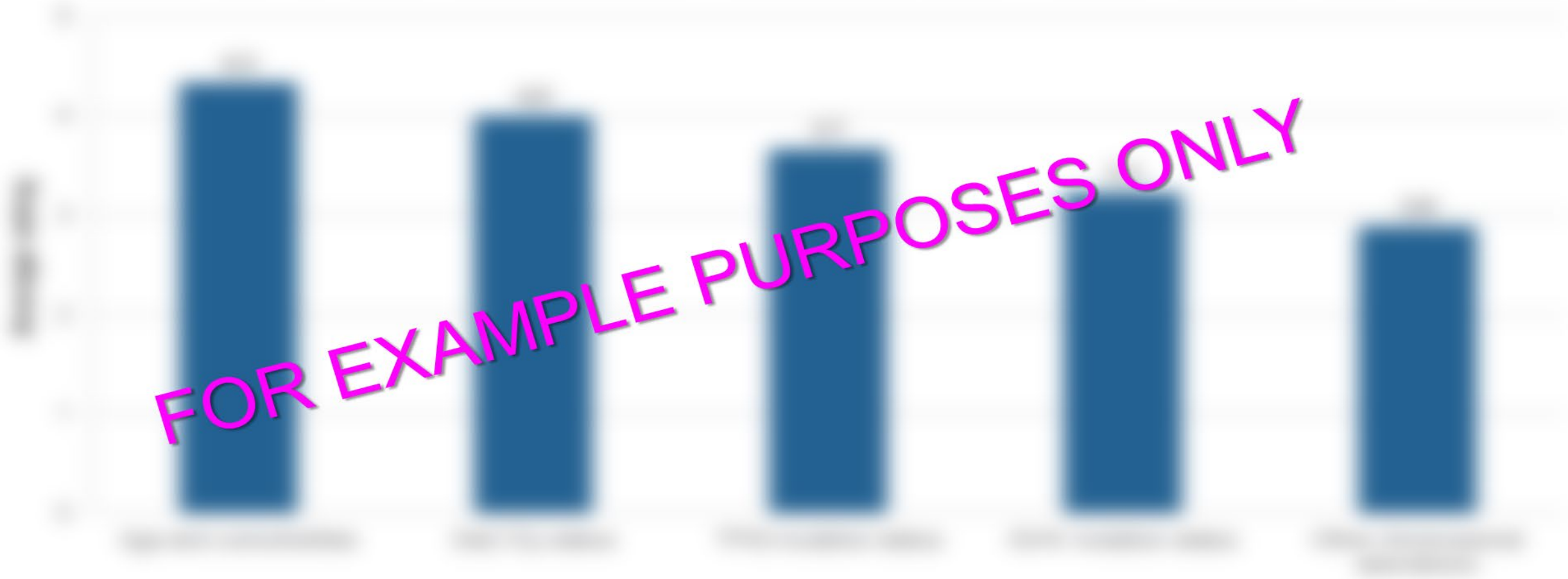
CASES

- The patient received a MUD-SCT after 3 cycles of augmented hyper-CVAD.

BLINATUMOMAB IS THE PREFERRED TREATMENT AFTER SCT FOLLOWED BY RELAPSED DISEASE IN THE PRESENTED PATIENT SCENARIO (N = 8)

CASES

What would you now recommend?



PATIENT CASE

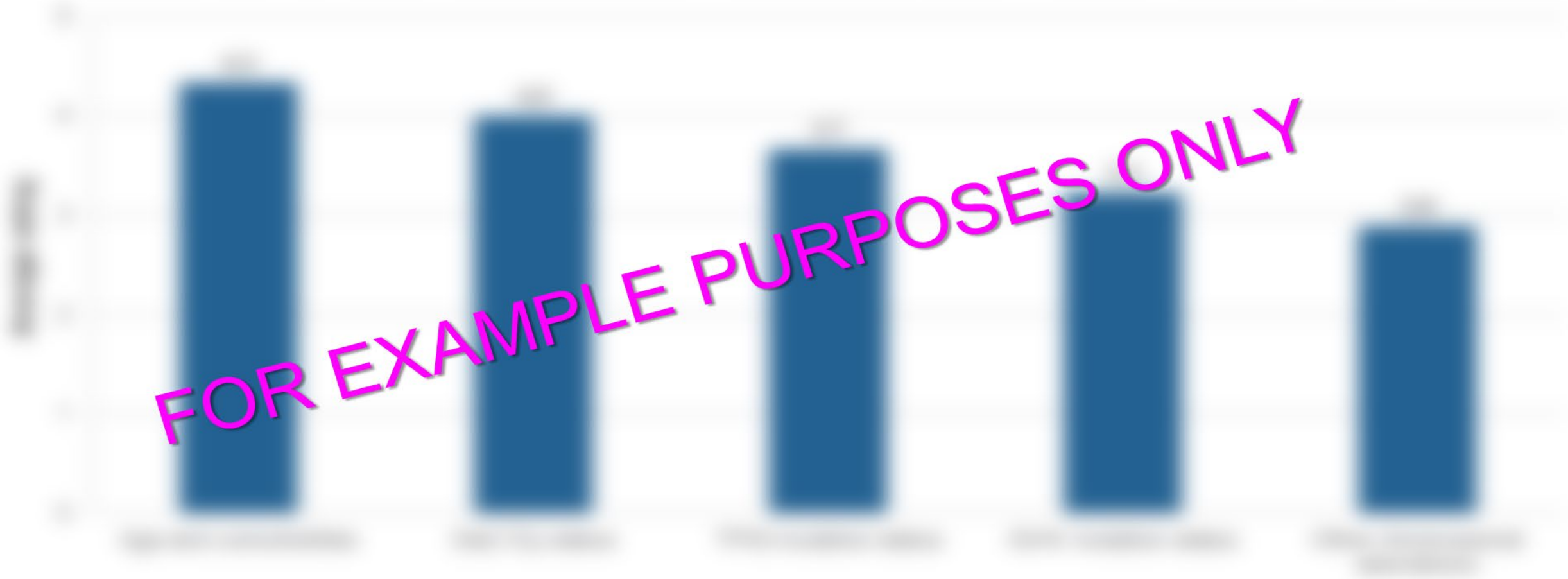
CASES

- Thirty-five-year-old female with history of pre–B-ALL diploid cytogenetics and

BLINATUMOMAB WOULD BE USED BY ALL THE ADVISORS IN THE DESCRIBED YOUNG PATIENT WHO RELAPSED AFTER CONSOLIDATION (N = 7*)

CASES

Your next plan would be:



*One advisor did not respond.

PATIENT CASE (CONTINUED)

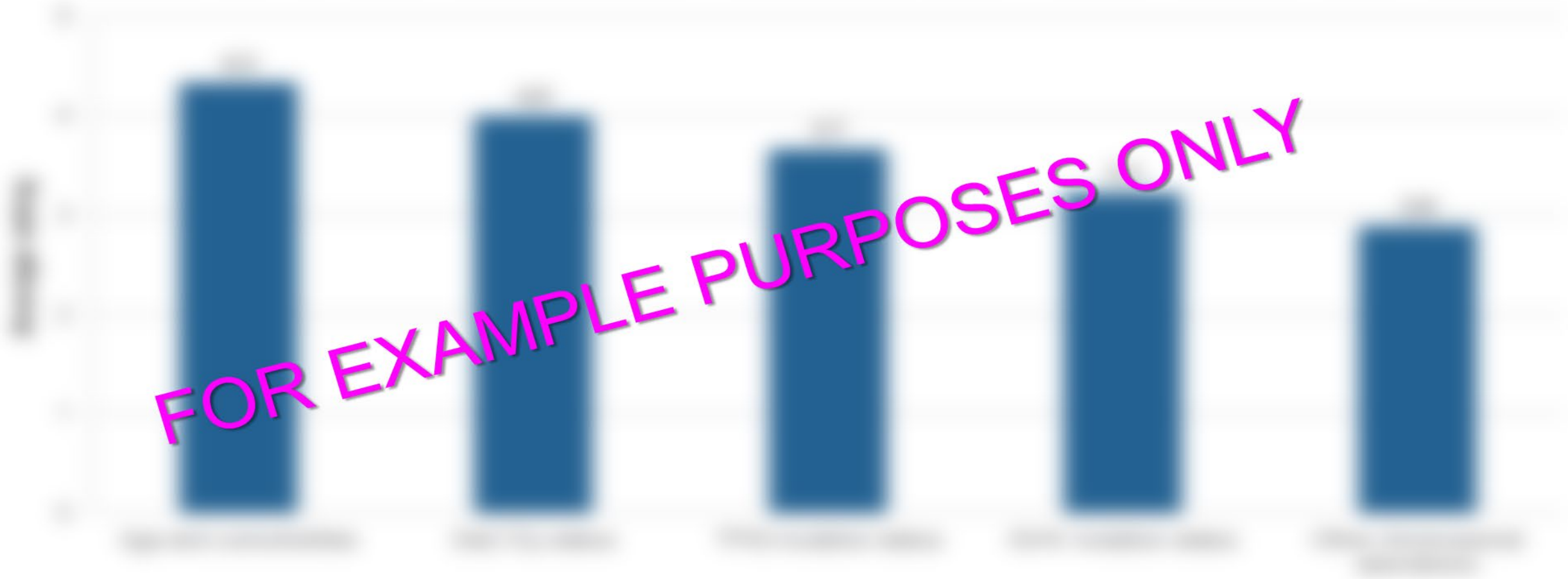
CASES

- Patient was reinduced with blinatumomab and achieved CR2 at day 28. MRD

CONSOLIDATION WITH ALLO-SCT IS THE PREFERRED TREATMENT STRATEGY FOR THE DESCRIBED PATIENT SCENARIO (N = 7*)

CASES

Your next plan would be:



*One advisor did not respond.