APTITUDE HEALTH®

CASES

INSIGHTS INTO ACUTE MYELOID LEUKEMIA (AML)

Friday, 21 May 2021

Virtual Program

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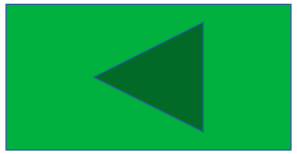
HOW TO NAVIGATE THIS REPORT

CASES

Click to move to topic of interest or ARS supporting data



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Advisor Key Takeaways
ARS Data

REPORT OBJECTIVES

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STUDY OBJECTIVES

- Gain perspectives on treatment practices in Italy, Germany, and Spain for adult patients with AML
- Gain insight into the influence of recent data and approvals on treatment practices

REPORT SNAPSHOT: SESSION OVERVIEW

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A moderated roundtable discussion with hematologists from Spain, Italy, and Germany was held virtually on **May 21, 2021***

Disease state and data presentations were led by **Prof Adriano Venditti** from Italy and **Prof Richard Schlenk** from Germany, and discussions were moderated by Prof Venditti

Insights were obtained on current and emerging treatment practices for adult patients with AML

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

*For the ARS questions, because the number of votes per country was not numerically high, country-to-country analysis of the data has not been done for this report.

ATTENDEE OVERVIEW* AND DEMOGRAPHICS

- The group of advisors comprised 15 hematologists with experience treating adult patients with AML from Spain (6), Italy (6), and Germany (3)

*All the participants could vote throughout the ARS questions, except the chair, therefore N=14.
**Two advisors did not respond; ^Three advisors did not respond.

AGENDA

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Time (PR/EST)	Topic
15.00 – 15.10	Introduction
15.10 – 15.25	First-Line Treatment of AML
15.25 – 17.00	Patient Case Presentations: First-Line Treatment of AML
17.00 – 17.15	Break
17.15 – 17.30	Management of Relapsed/Refractory (R/R) AML and Promising Strategies
17.30 – 18.05	Patient Case Presentations: R/R AML
18.05 – 18.25	Key Takeaways and Meeting Evaluation
18.25 – 18.30	Meeting Close

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Topline Takeaways and Strategic Recommendations

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS

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OBJECTIVES

- 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

PROCESS

Through ARS questions and moderated discussions, community oncologists described their testing practices and challenges they experience

INSIGHTS

- 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 ORR
- 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

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Key Insights and Discussion Summary

DISCUSSION: TREATMENT OF AML

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INSIGHTS

[R/R AML] *"I think it is mandatory to re-evaluate the molecular status, even if it is only after 1 cycle,*

- Treatment success in frontline DLBCL

- Data needed to switch from SOC in frontline

DISCUSSION: TREATMENT OF AML

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INSIGHTS

"For nearly 30 years we have said if a patient is fit for intensive chemotherapy, we should use

- [illegible]

[illegible]

- [illegible]

[illegible]

DISCUSSION: TREATMENT OF AML

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INSIGHTS

"We know that MRD is a negative prognostic factor for the outcome of an allogeneic bone marrow

- [illegible]

- [illegible]

DISCUSSION: TREATMENT OF AML

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INSIGHTS

"This kind of patient is not a good candidate for standard chemo because a transplant is not an

- [illegible]
- [illegible]

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Advisor Key Takeaways

ADVISOR KEY TAKEAWAYS*

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ADVISOR		ADVISOR	
1	> New agents are improving the outcome and the > I have a better understanding of sequencing therapies > I really wasn't that familiar with proteasomals and tallestamab but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> I think one key message would be that we got a lot of novel > For relapsed/refractory patients it's nice to have different options besides R-CD and auto or going to CAR T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the talledtamab and hope that tafa and Rec would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like proteasomals that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
3	> It was great to hear about innovations and what's coming down the pipeline for relapsed/refractory	7	> Very interesting to learn about all these relapsed/refractory treatments, specifically the bispecific antibodies > A lot of options coming up in the future. The only issue will be to learn how to sequence these drugs
4	> There's a lot of good options for second line than just CAR T and transplant with decent side effect profile and good response rates > Sequencing is an issue	8	> Still R-CHOP is the standard

Two advisors did not respond. Chair and speakers did not provide key takeaways.

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ARS Data – Management of AML

ADVISORS VALUE EQUALLY ALL METHODS TO RISK-STRATIFY THEIR NEWLY DIAGNOSED AML PATIENTS

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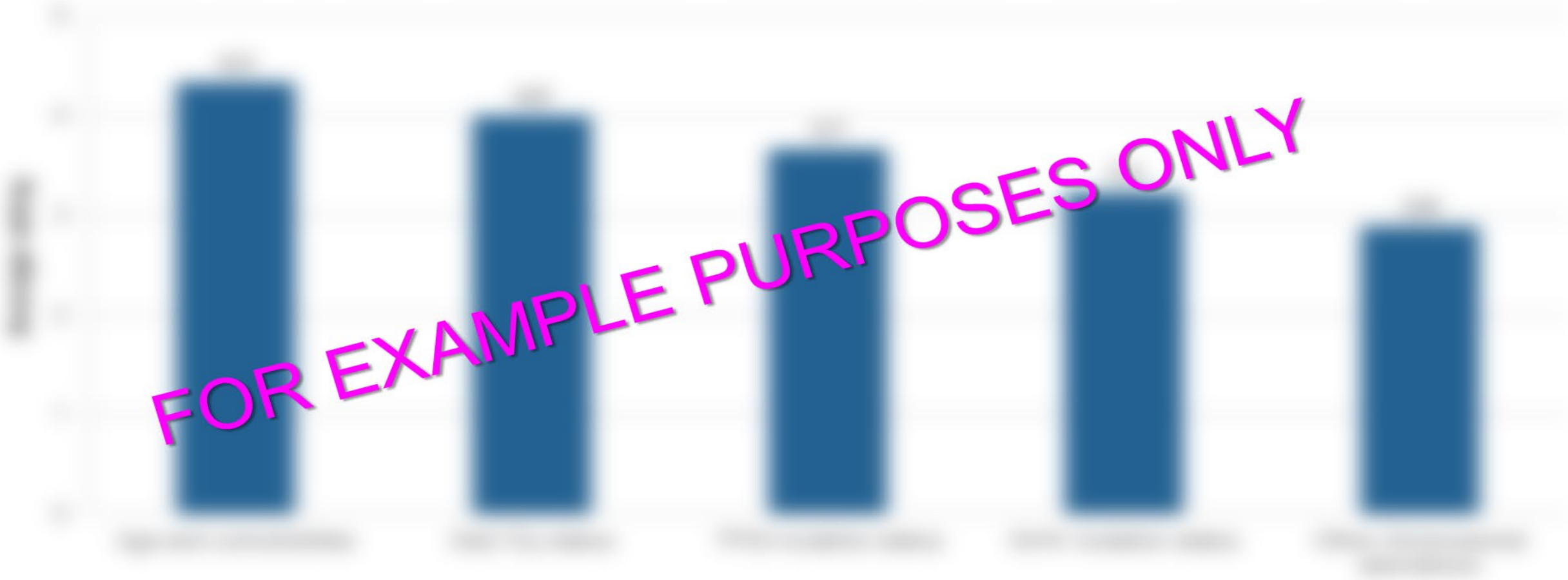
If you risk-stratify your newly diagnosed AML patients, what method do you use? (Select all that apply.) (n = 10*)



FOR EXAMPLE PURPOSES ONLY

*Four advisors did not respond.

FOR MOST OF THE ADVISORS, >21% OF THEIR AML PATIENTS ARE 75 YEARS OR OLDER

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What percentage of your AML patients are 75 years or older? (n = 11*)

FOR EXAMPLE PURPOSES ONLY

*Three advisors did not respond.

FOR MOST OF THE ADVISORS, <20% OF THEIR AML PATIENTS ARE UNDER 75 YEARS WITH COMORBIDITIES THAT PREVENT USE OF INTENSIVE INDUCTION CHEMOTHERAPY

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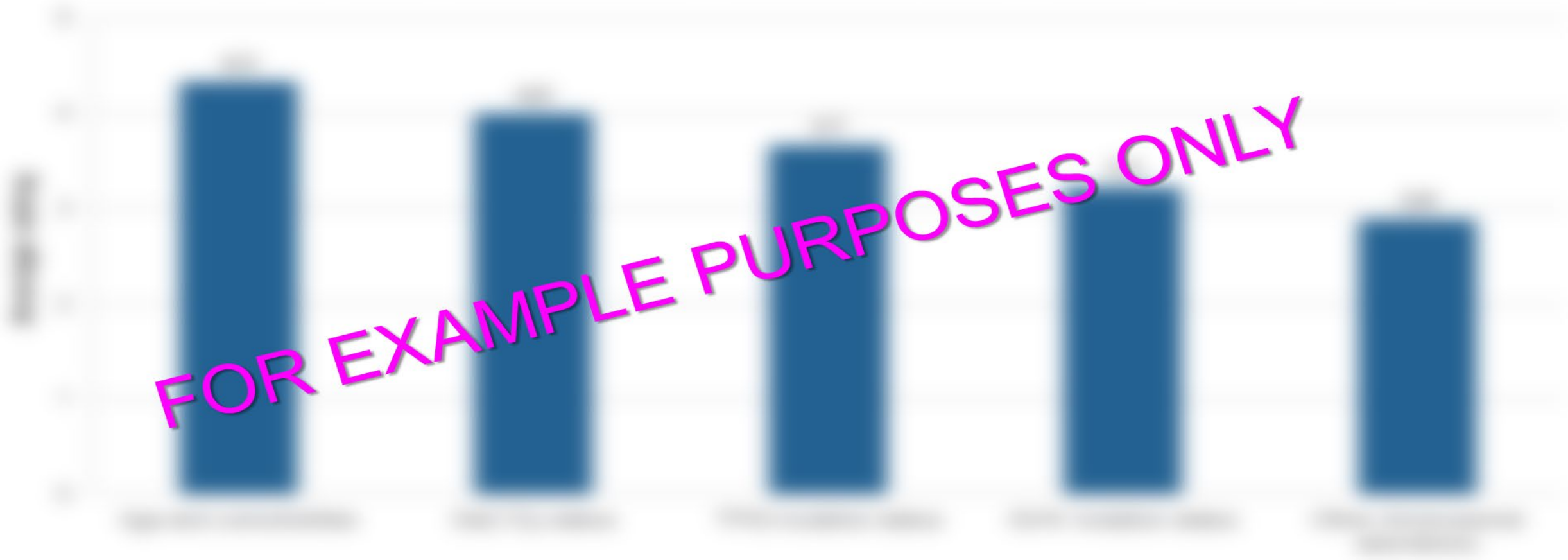
What percentage of your AML patients are under 75 years old, but have comorbidities that prevent use of intensive induction chemotherapy? (n = 11*)



FOR EXAMPLE PURPOSES ONLY

*Three advisors did not respond.

ADVISORS PLACE EQUAL VALUE ON ALL THE MOLECULAR MARKERS ROUTINELY TESTED FOR THEIR NEWLY DIAGNOSED AML PATIENTS

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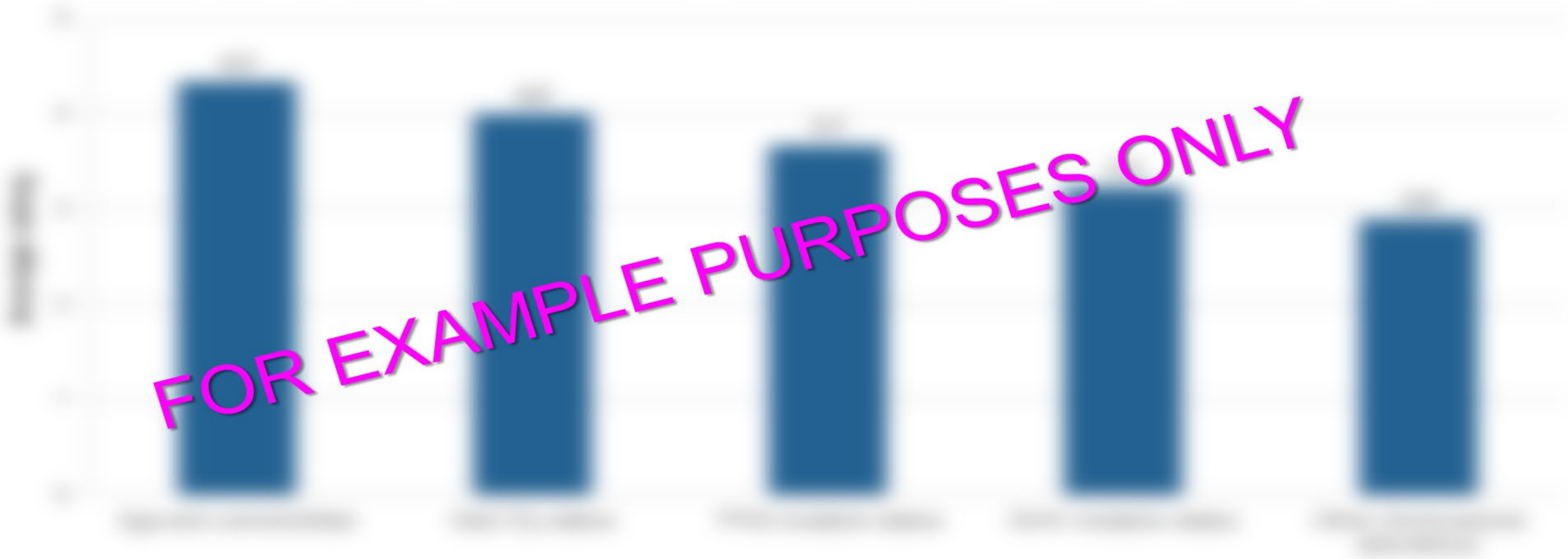
In addition to cytogenetics, which of the following molecular markers are you routinely testing for in your newly diagnosed AML patients? (Select all that apply.) (n = 12*)



FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

MOST OF THE ADVISORS TEST THE SAMPLE IN THEIR LOCAL HOSPITAL

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When it comes to molecular/genomic testing: (n = 14)

FOR EXAMPLE PURPOSES ONLY

FOR THE MAJORITY OF ADVISORS, THE TURNAROUND TIME OF GENOMIC/MUTATIONAL TESTING IS <7 DAYS

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When it comes to genomic/mutational testing, the turnaround time to get the final results is: (n = 14)

FOR EXAMPLE PURPOSES ONLY

MORE THAN HALF OF THE ADVISORS SOMETIMES START AML FRONTLINE THERAPY BEFORE THE GENOMIC/MUTATIONAL TEST RESULTS ARE AVAILABLE

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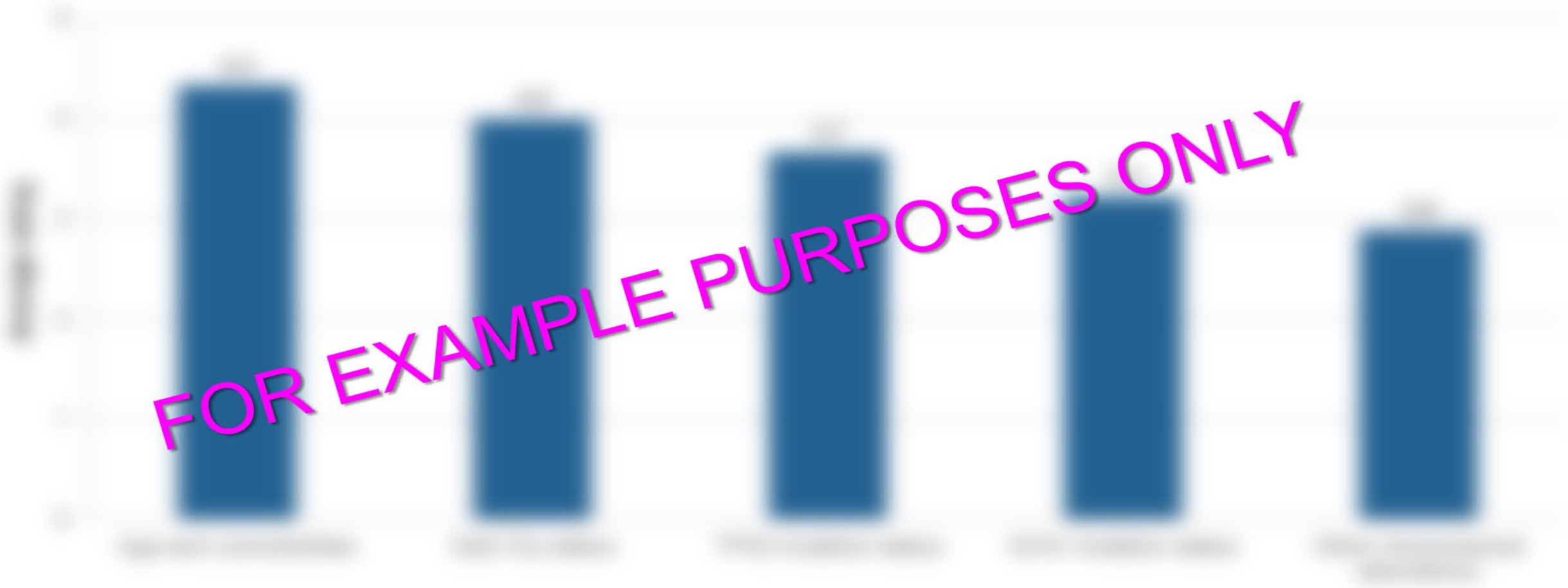
In general, the following statement describes me best: (n = 14)



FOR EXAMPLE PURPOSES ONLY

ALL THE ADVISORS USE MRD TO GUIDE THEIR TREATMENT DECISIONS IN AML

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Do you use MRD to guide your treatment decisions in AML? (n = 14)

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ARS Data – Management of R/R AML

THE MAJORITY OF ADVISORS ROUTINELY REPEAT BIOMARKER TESTING IN THEIR AML PATIENTS AT THE TIME OF RELAPSE

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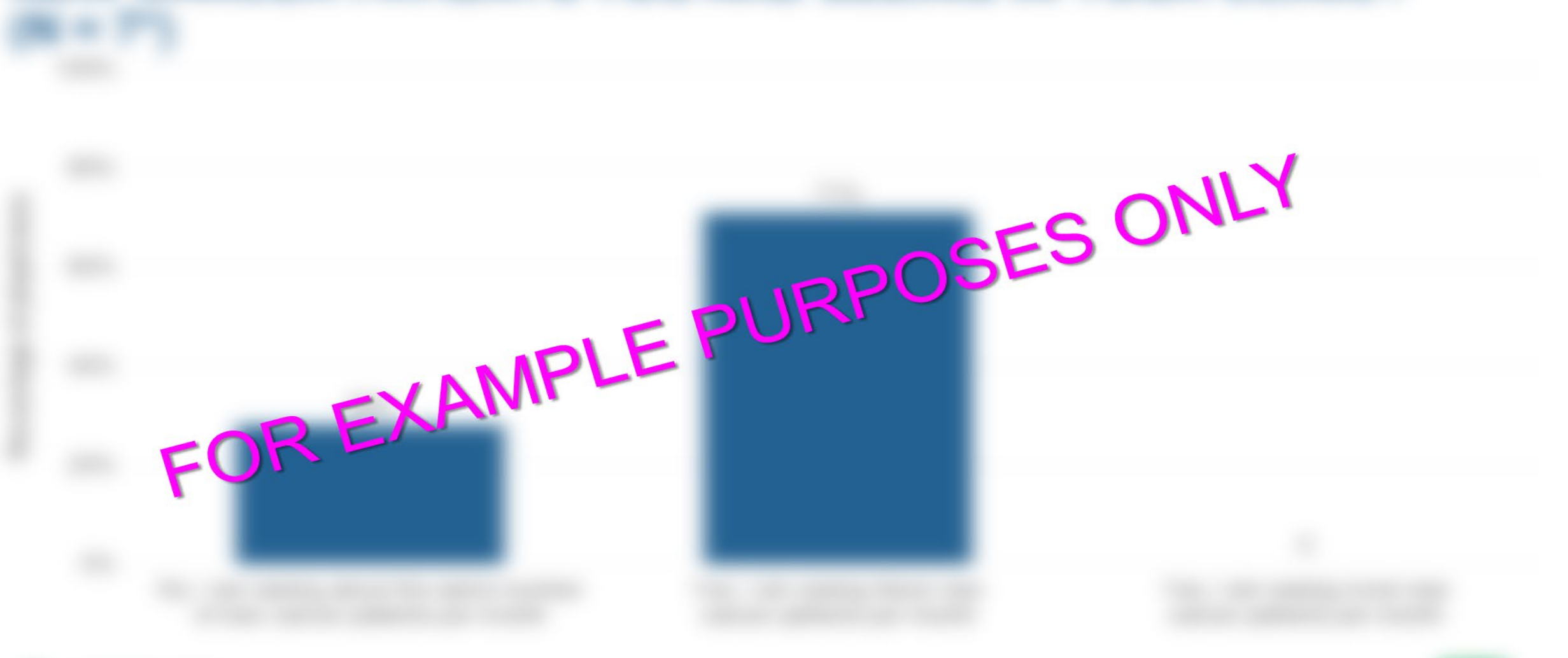

FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

ALL OF THE ADVISORS THINK *IDH1/2* AND *FLT3* ARE THE MOST IMPORTANT MUTATIONS TO CHECK IN PATIENTS WITH RELAPSED AML, FOR THERAPEUTIC DECISION-MAKING

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FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.

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Patient Cases

PATIENT CASE 1: *FLT3* MUTATION, ELIGIBLE FOR INTENSIVE CHEMO

NEWLY DIAGNOSED AND R/R AML

PATIENT CASE 1: *FLT3* MUTATION, ELIGIBLE FOR INTENSIVE CHEMO

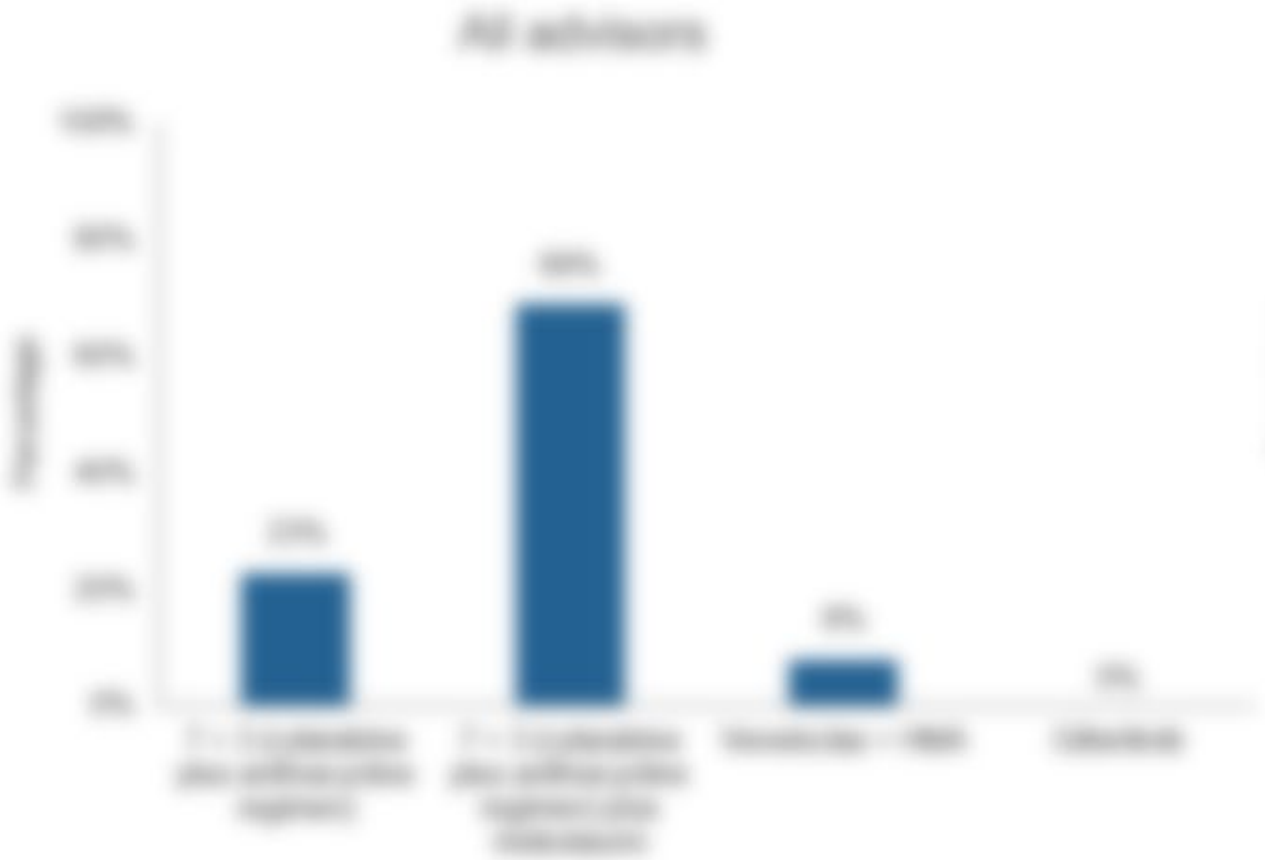
CASES

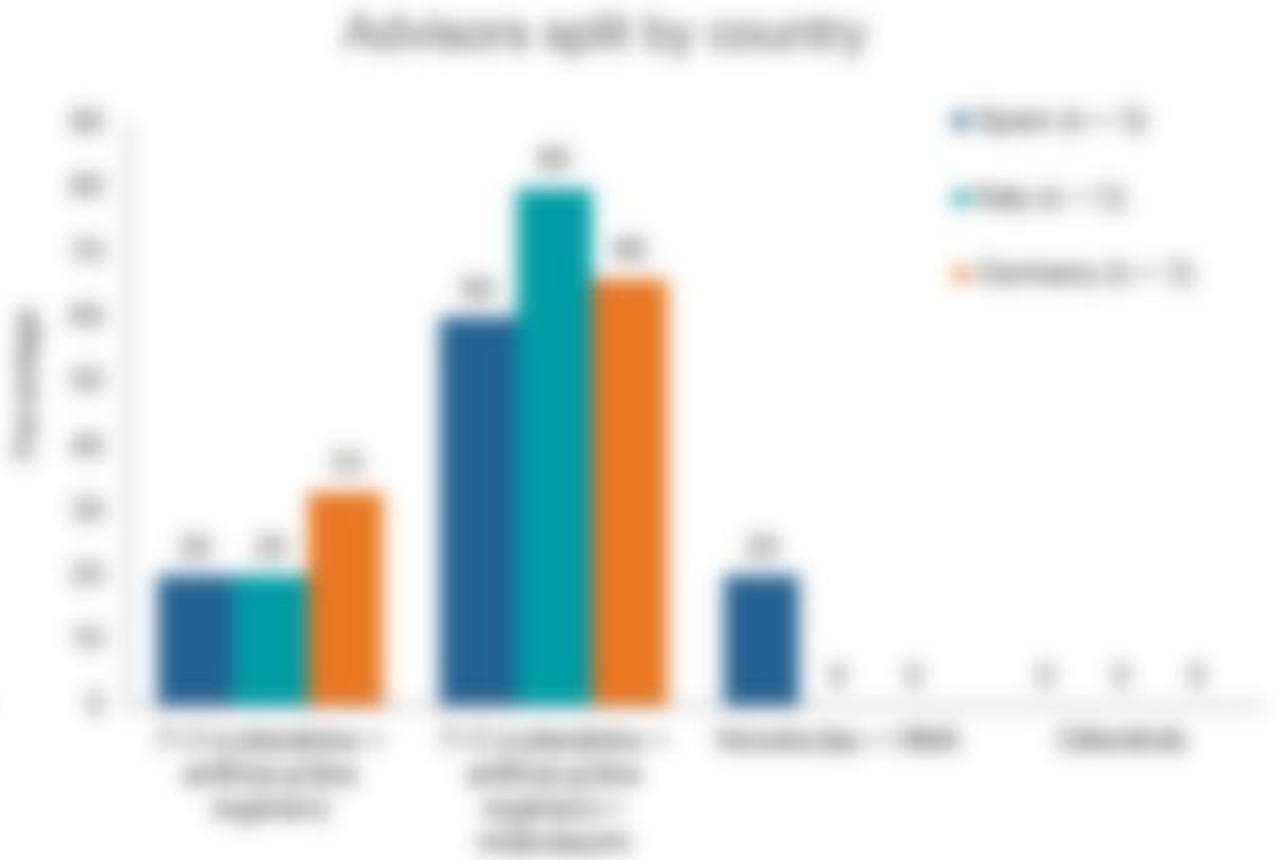
- Patient characteristics

THE MAJORITY OF ADVISORS WOULD CHOOSE 7 + 3 + MIDOSTAURIN AS FRONTLINE TREATMENT FOR THIS PATIENT

CASES

Which frontline treatment should be performed? (n = 13*)





*One advisor did not respond.

FOR THE MAJORITY OF ADVISORS, OVERALL SURVIVAL IS THE ENDPOINT FOR THIS PATIENT

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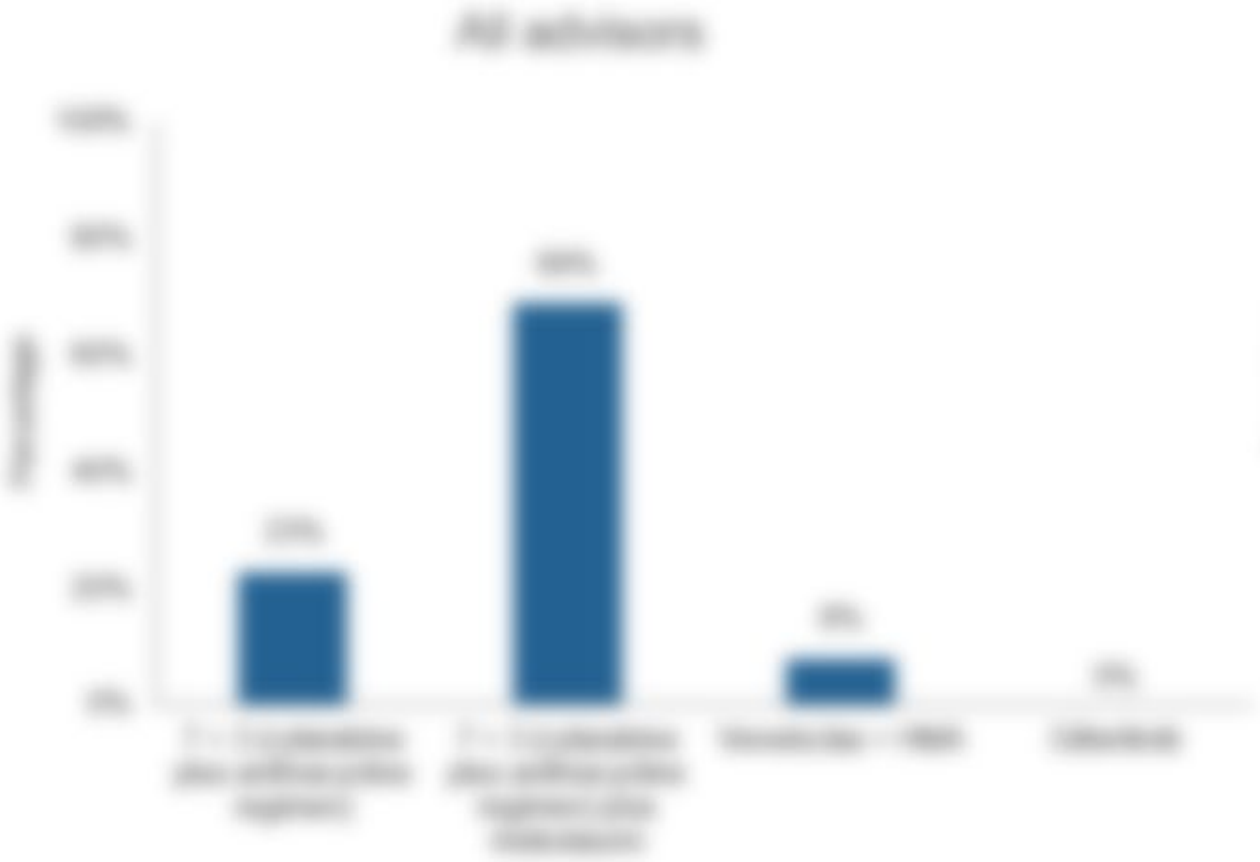
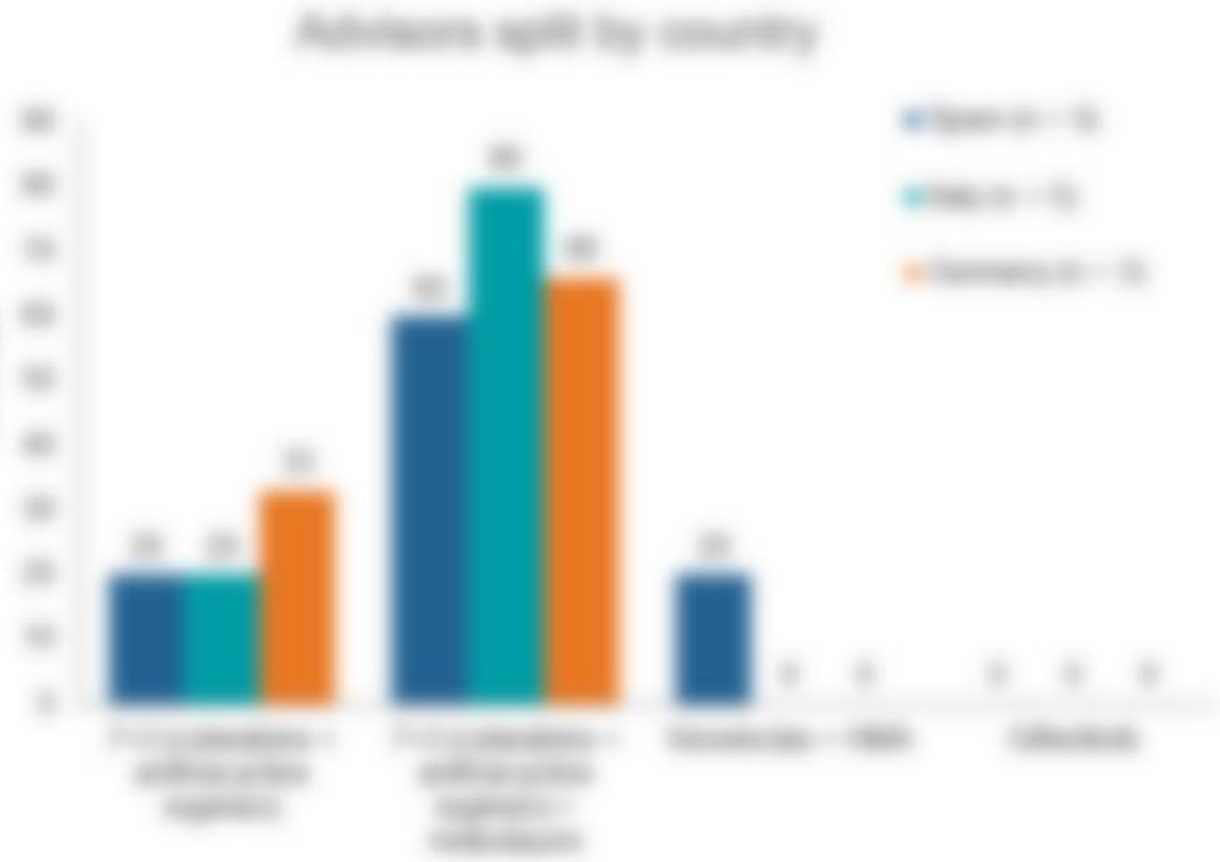
Which is the endpoint in this patient? (n = 14)





PATIENT CASE 1: *FLT3* MUTATION, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

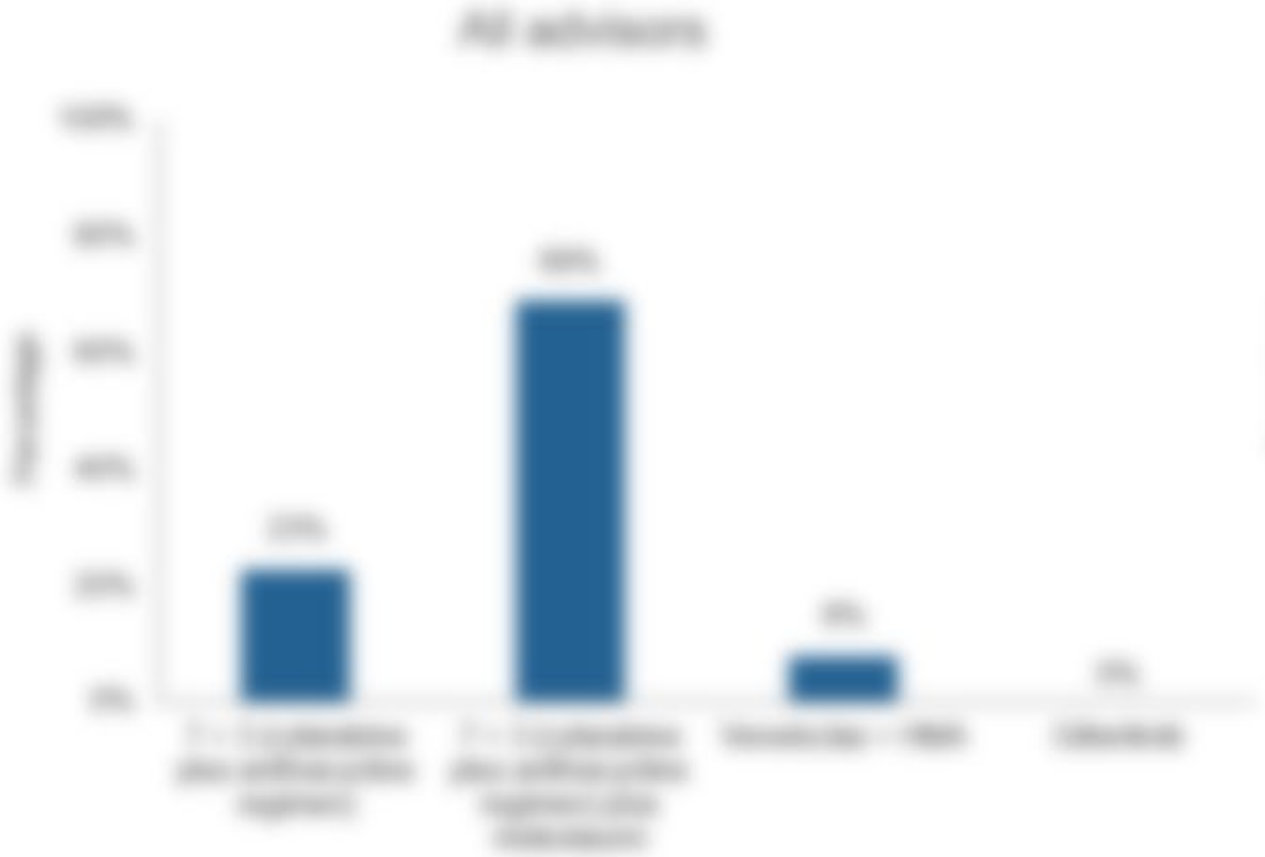
CASES

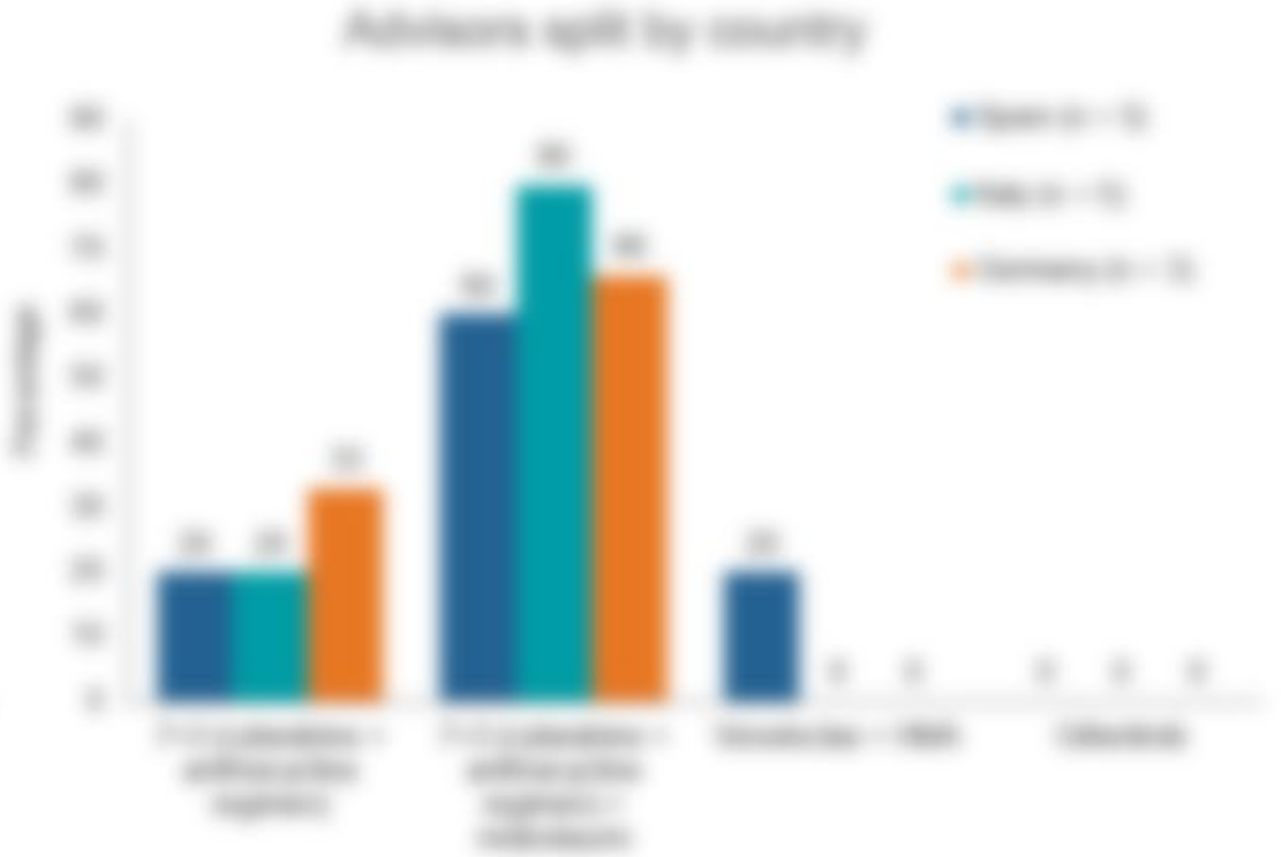
- Frontline therapy

THE MAJORITY OF ADVISORS WOULD CHOOSE GILTERITINIB FOR THIS PATIENT, IN THE RELAPSED SETTING

CASES

What would be the best option now? (n = 13*)





*One advisor did not respond.

PATIENT CASE 1: *FLT3* MUTATION, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

- R/R therapy

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Patient Cases

PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY

NEWLY DIAGNOSED AND R/R AML

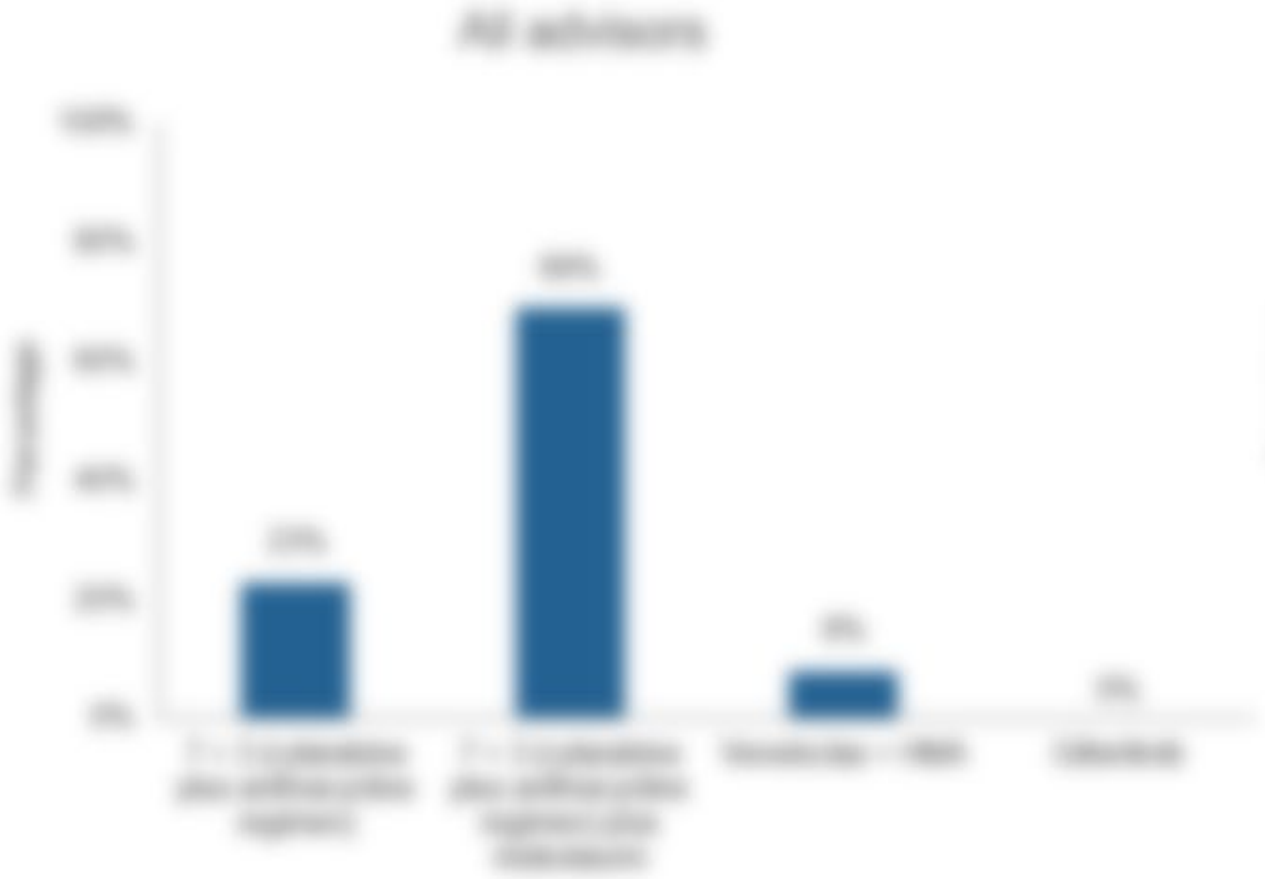
PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY

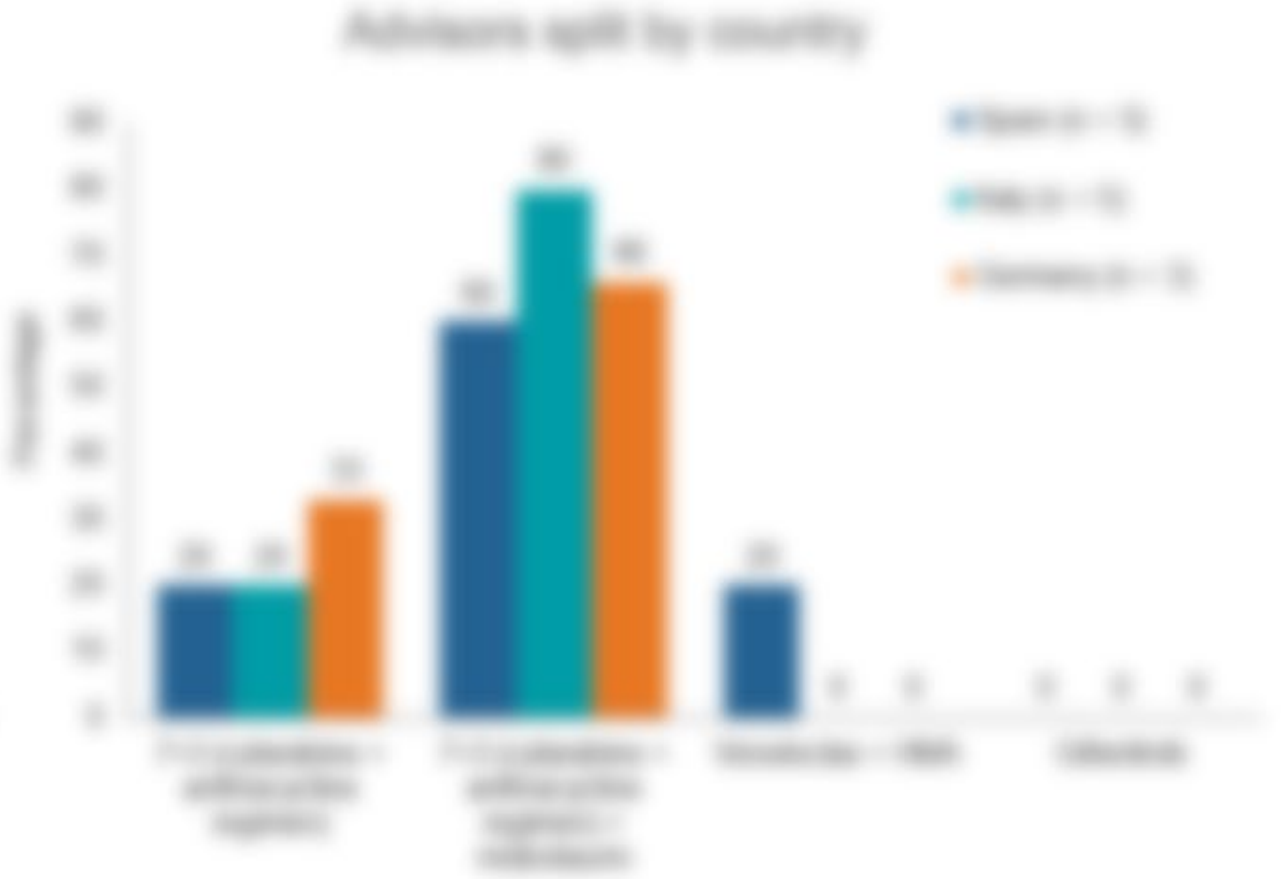
CASES

- Patient characteristics

OVER HALF OF ADVISORS WOULD CHOOSE AZACITIDINE, ALONE OR WITH VENETOCLAX OR VENETOCLAX + POSACONAZOLE AS INDUCTION FOR THIS PATIENT

CASES





*One advisor did not respond.

PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY, CONT.

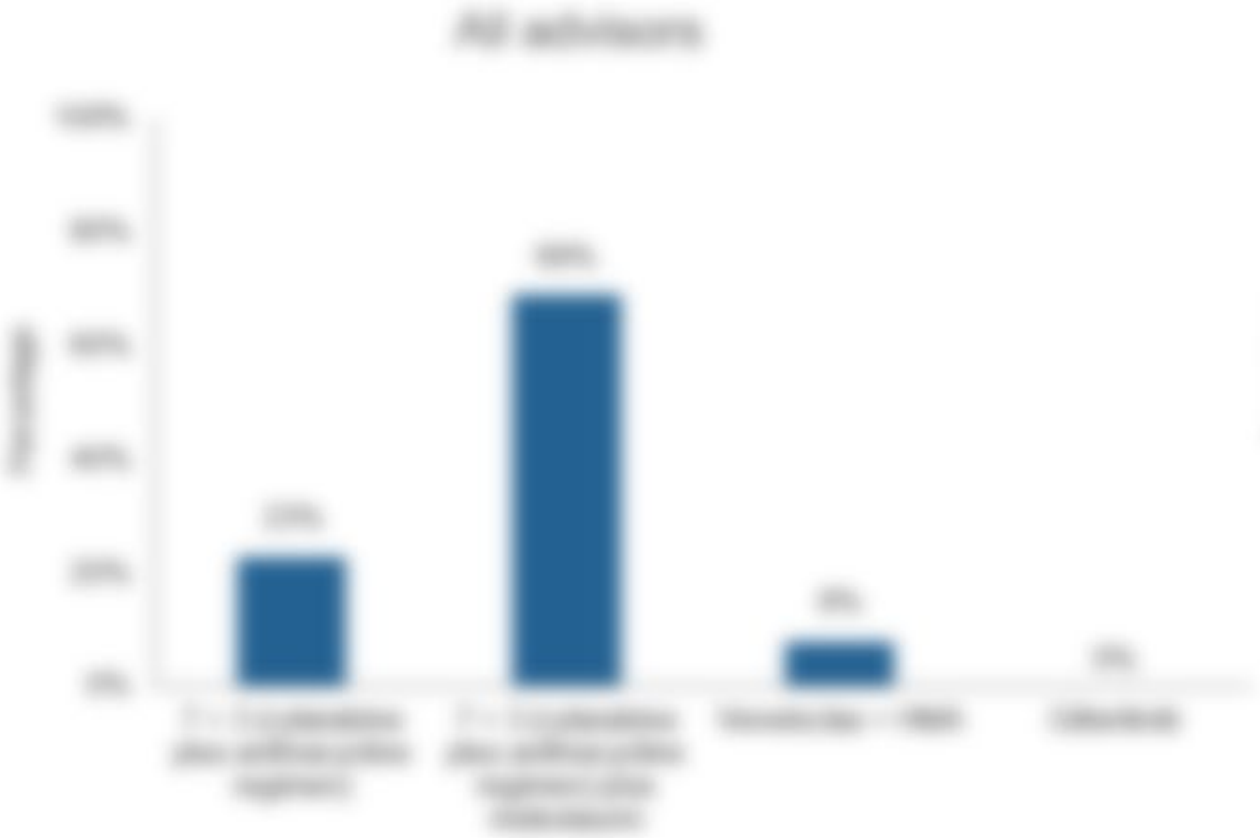
CASES

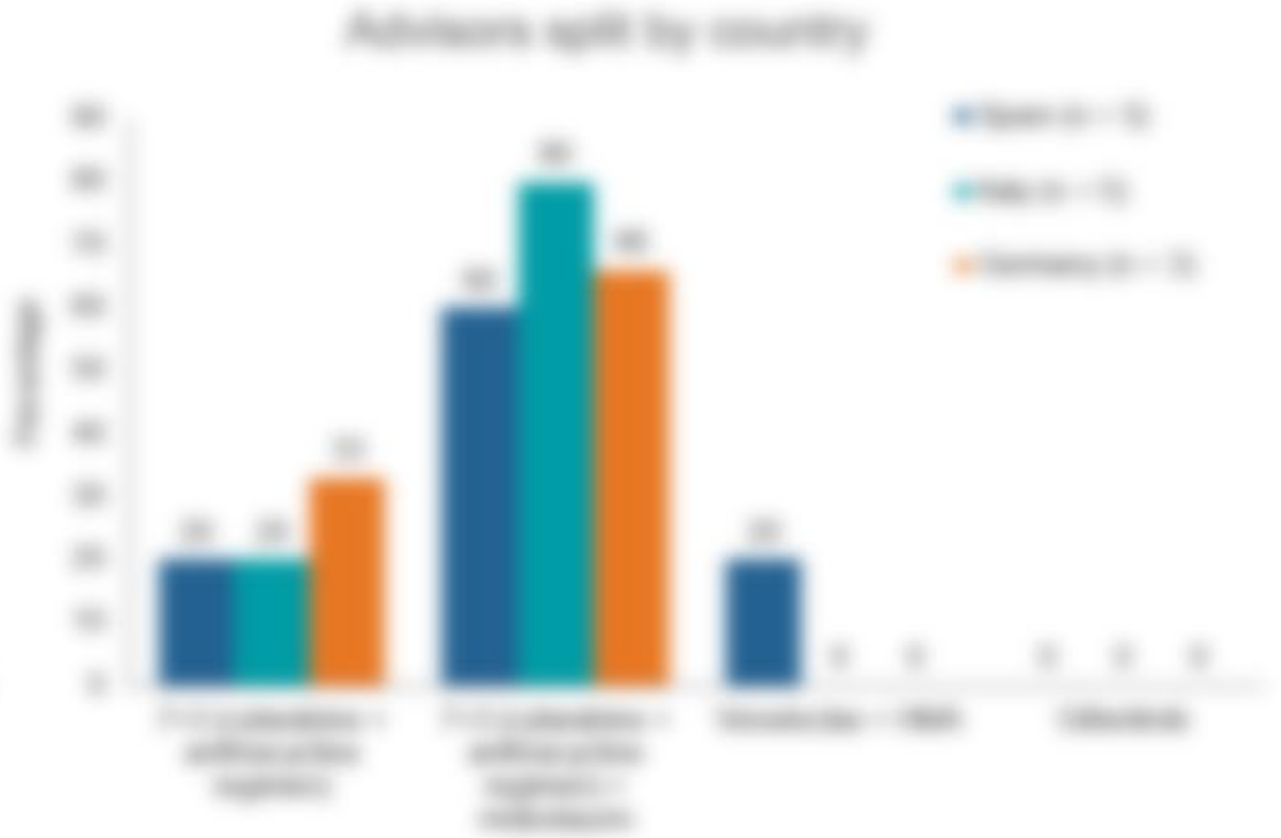
- Frontline therapy

HALF OF ADVISORS WOULD CHOOSE AZACITIDINE WITH VENETOCLAX OR VENETOCLAX + POSACONAZOLE, AS SECOND INDUCTION FOR THIS PATIENT

CASES

Which further therapy would you recommend? (n = 12*)





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*Two advisors did not respond.

PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY, CONT.

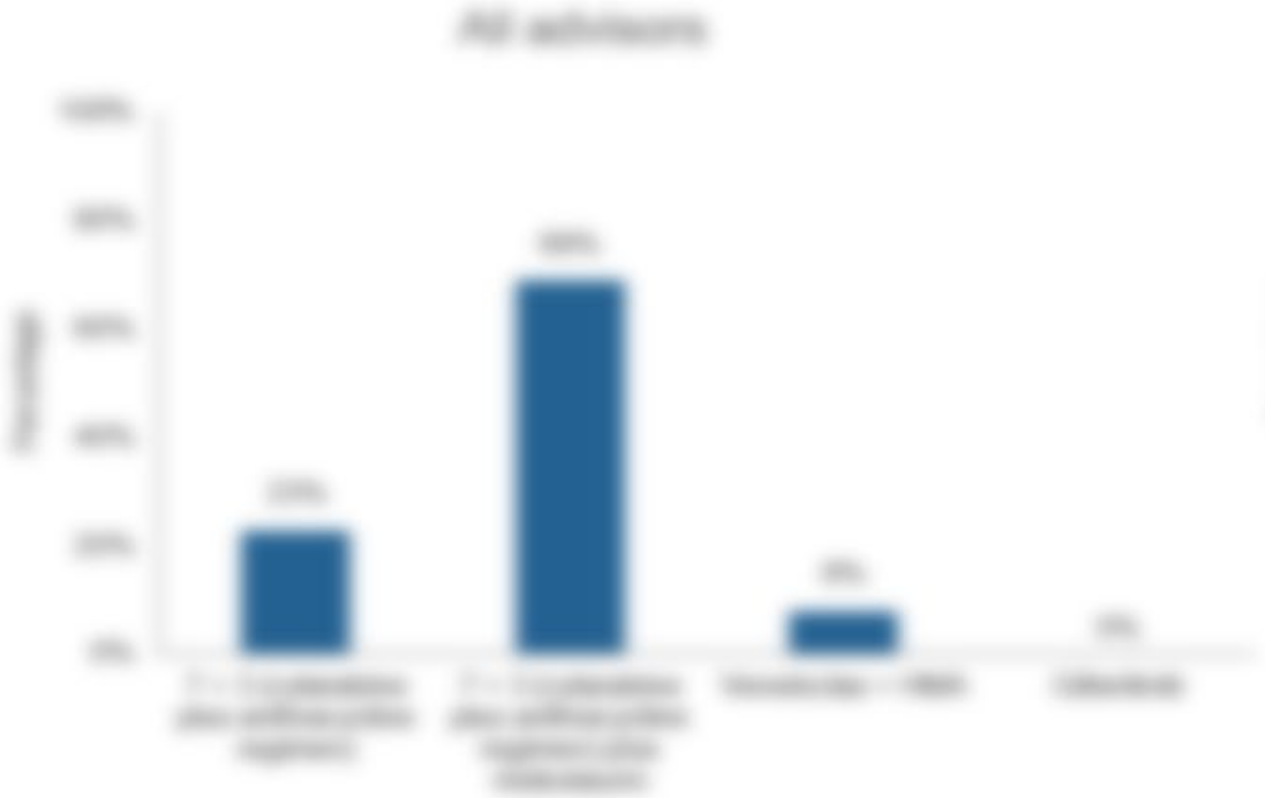
CASES

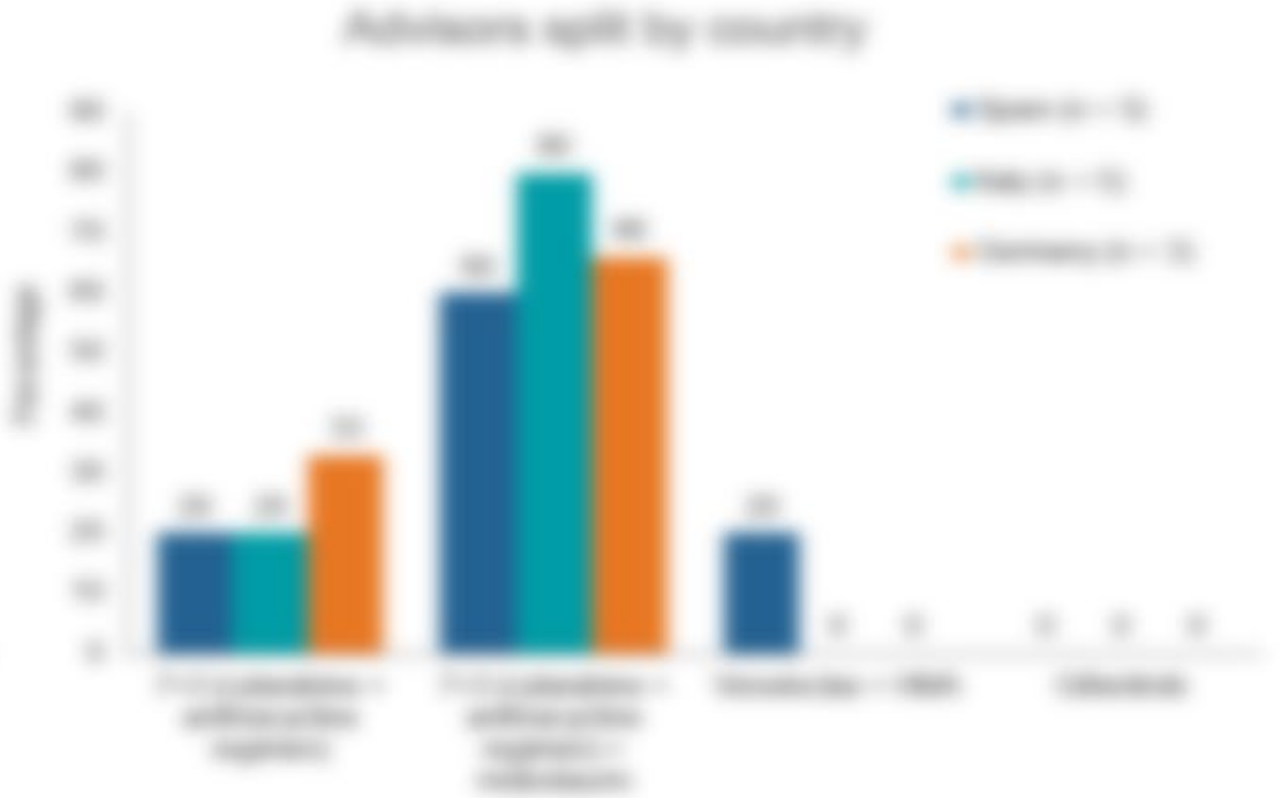
- Second induction

THE MAJORITY OF ADVISORS WOULD CHOOSE AZACITIDINE WITH VENETOCLAX OR VENETOCLAX + POSACONAZOLE AS CONSOLIDATION FOR THIS PATIENT

CASES

Which consolidation therapy would you recommend? (n = 13*)





*One advisor did not respond.

PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY, CONT.

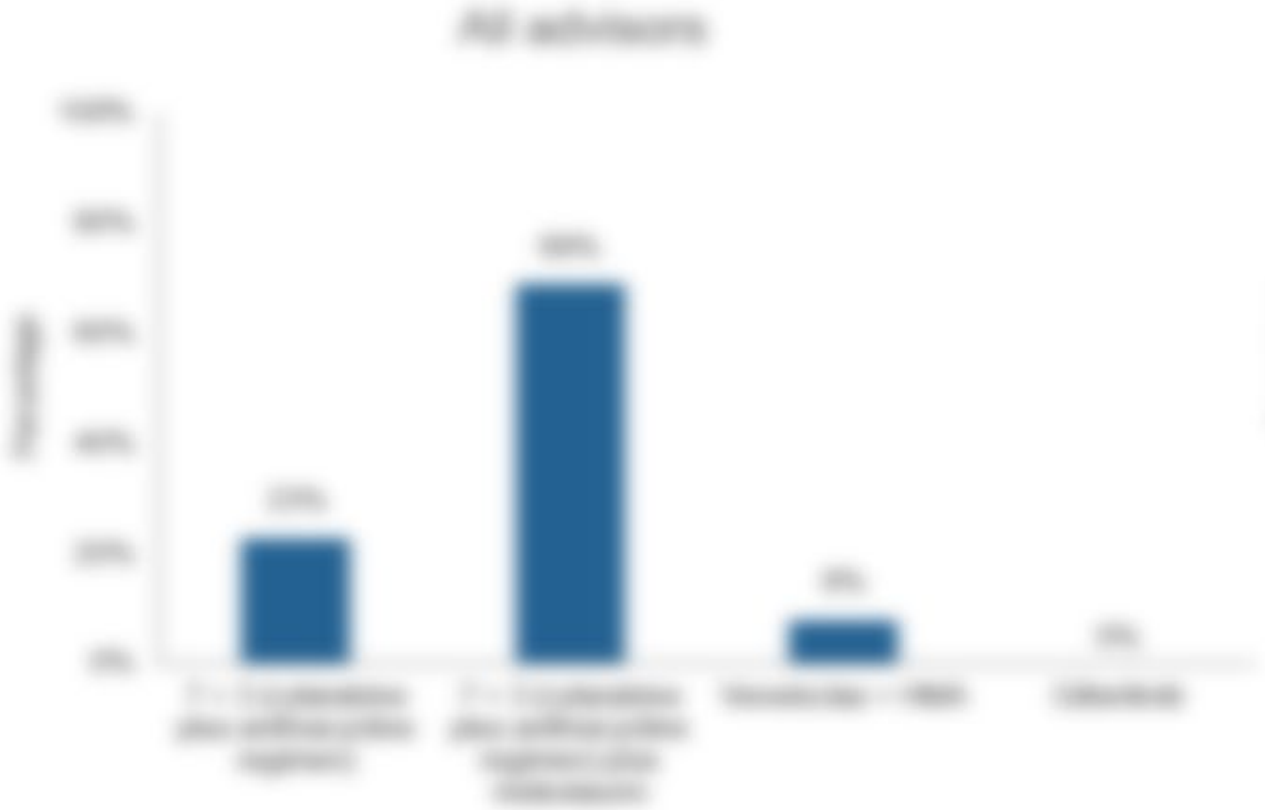
CASES

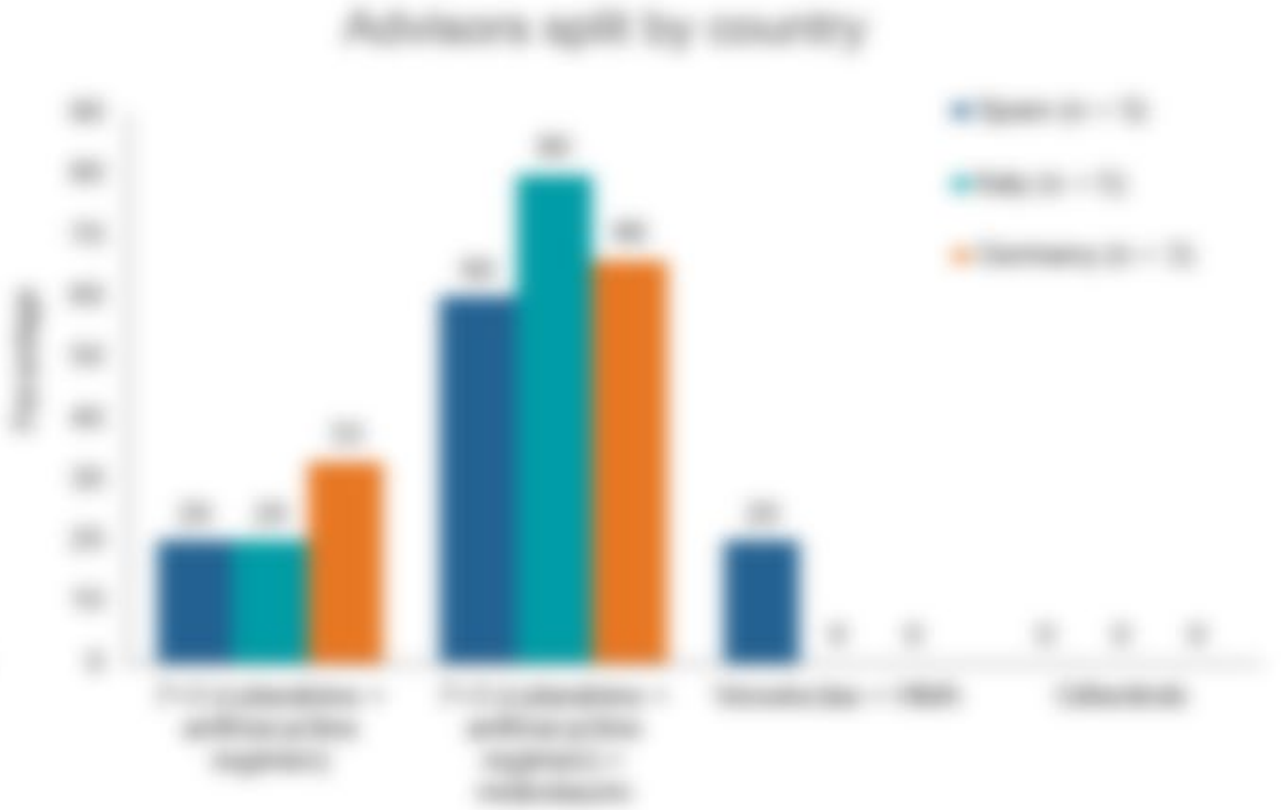
- Consolidation therapy

ALL OF THE ADVISORS WOULD CHOOSE AZACITIDINE ALONE OR IN COMBINATION WITH VENETOCLAX FOR THIS PATIENT, IN THE RELAPSED SETTING

CASES

Which treatment options should be discussed with the patient? (n = 5*)





*Nine advisors did not respond.

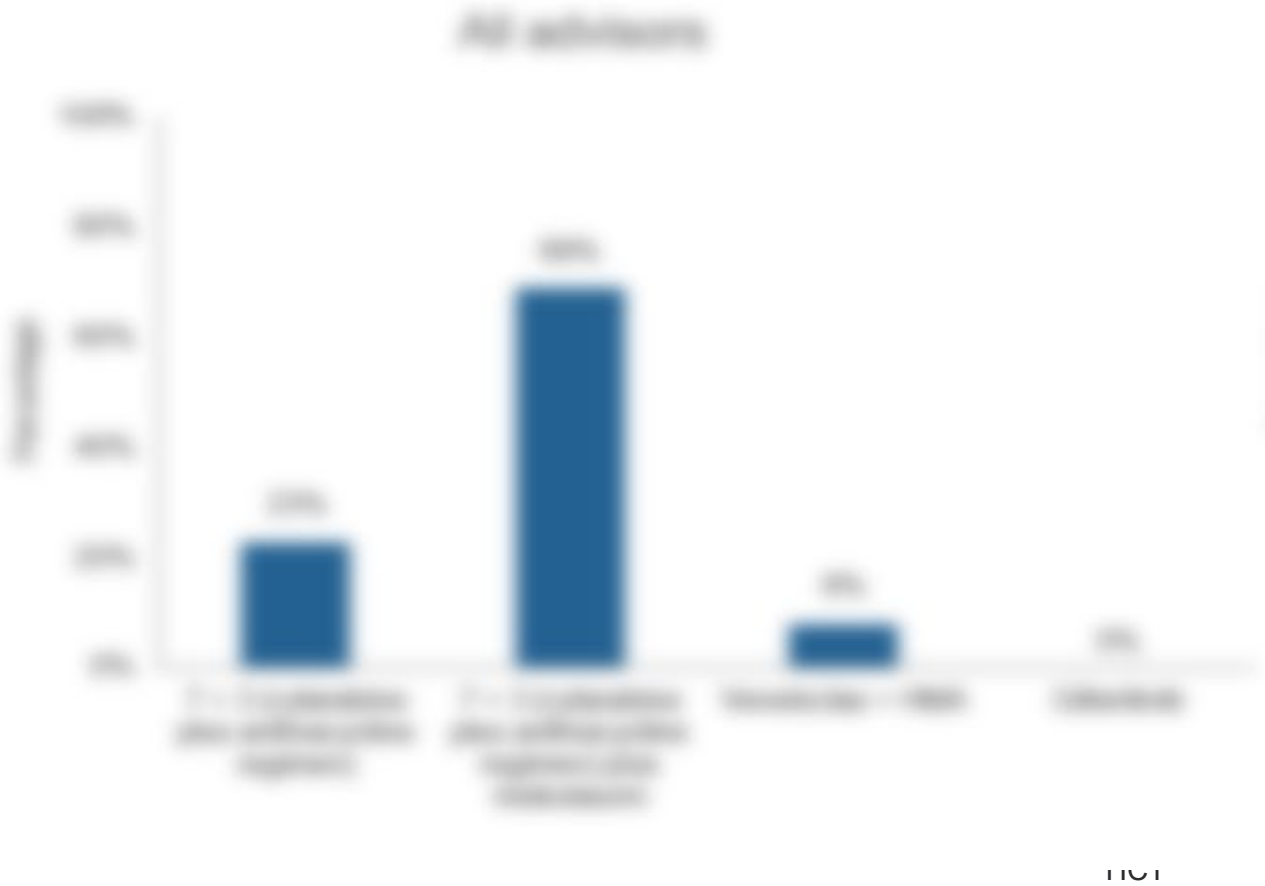
PATIENT CASE 2: INTERMEDIATE RISK, CD33 POSITIVE, ELIGIBLE FOR INTENSIVE CHEMOTHERAPY, CONT.

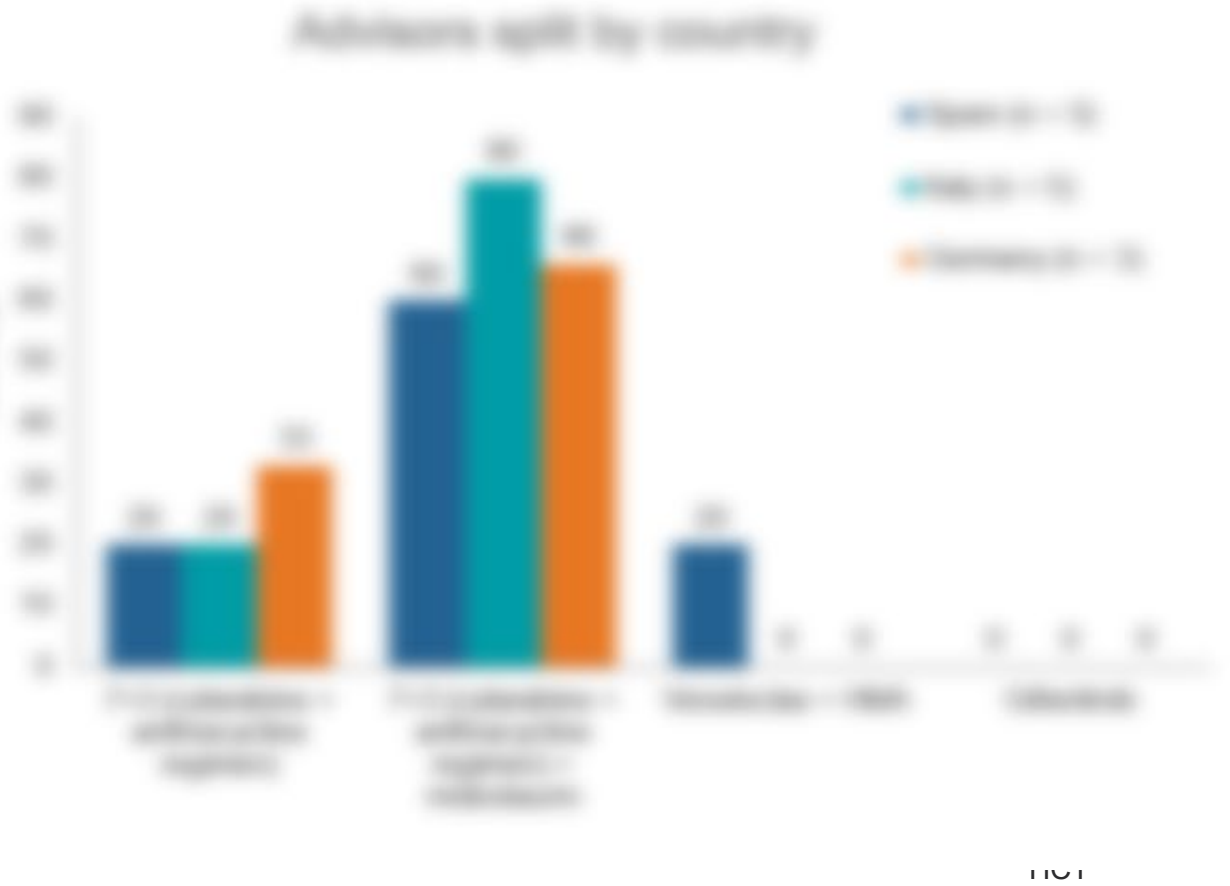
CASES

- Patient currently receiving azacitidine (75 mg/m², days 1–7) + venetoclax (400 mg/day)

THE MAJORITY OF ADVISORS WOULD THEN OPT FOR ALLOGENEIC STEM CELL TRANSPLANT, REGARDLESS OF MRD POSITIVITY

Would you move to allo-HCT, and when? (n = 3*)





HCT HCT

*Eleven advisors did not respond.

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Patient Cases

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO

NEWLY DIAGNOSED AML

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO

CASES

- Patient characteristics

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

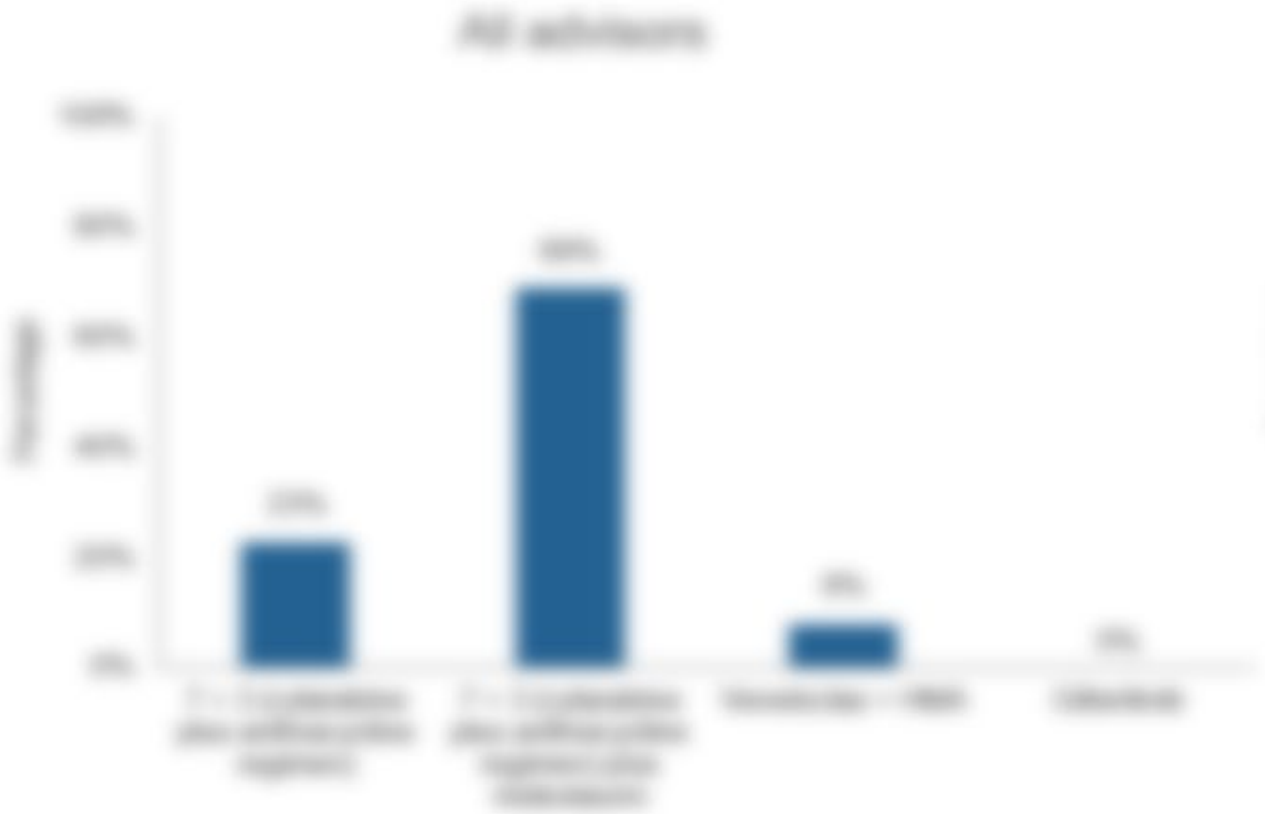
CASES

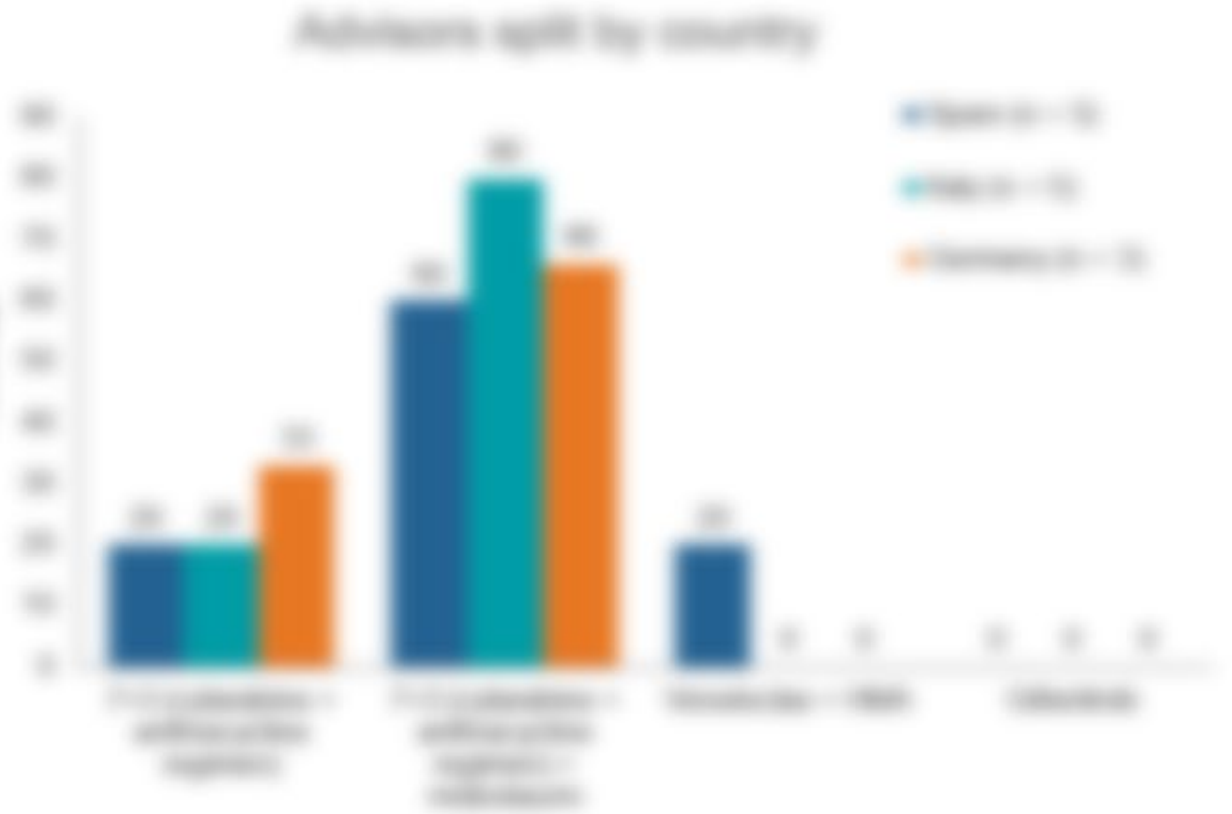
- Bone marrow assessment

OVER HALF OF THE ADVISORS WOULD CHOOSE CPX-351 AS FRONTLINE THERAPY FOR THIS PATIENT

CASES

Which first-line treatment would you choose? (n = 13*)





*One advisor did not respond.

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

> Frontline therapy

ALMOST HALF OF THE ADVISORS WOULD CONSIDER CHANGING ANTIFUNGAL TREATMENT (SERUM POSACONAZOLE BELOW THE THRESHOLD) FOR THIS PATIENT

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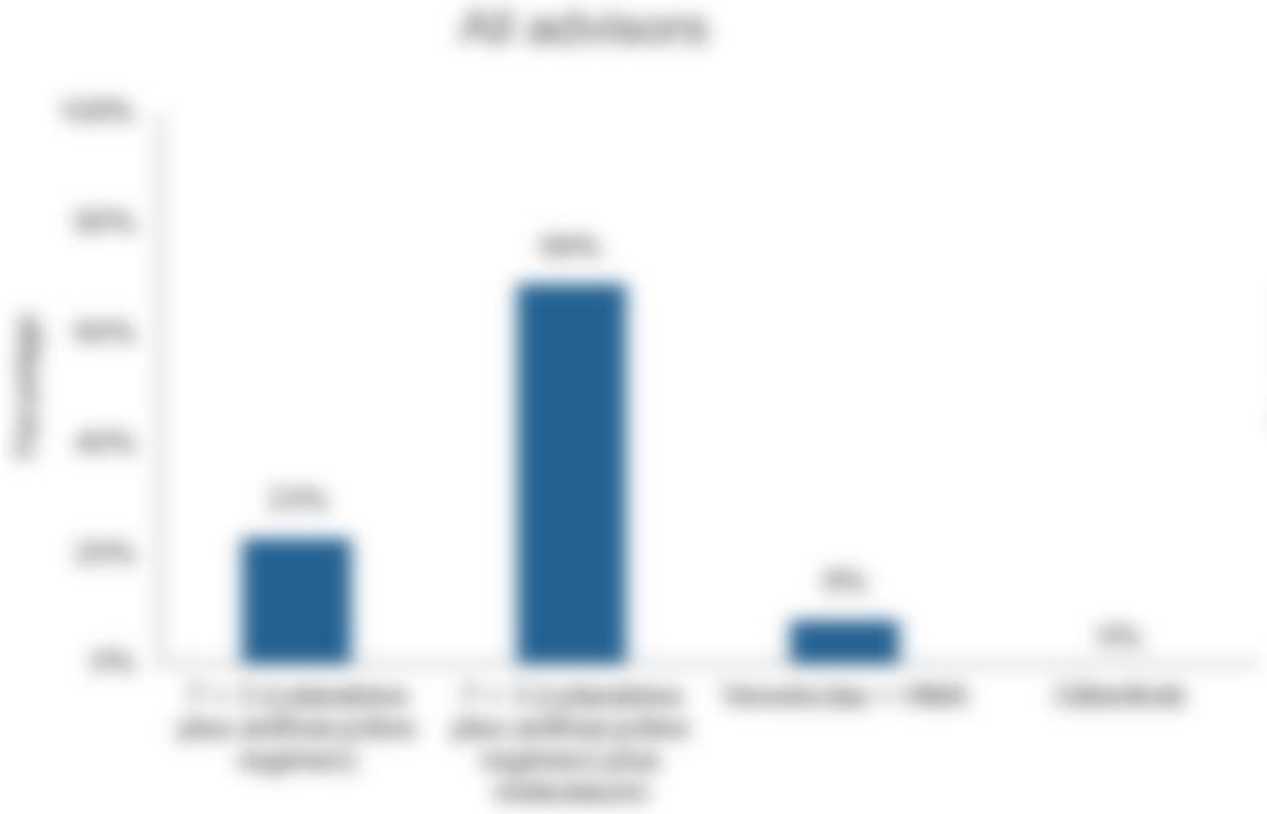
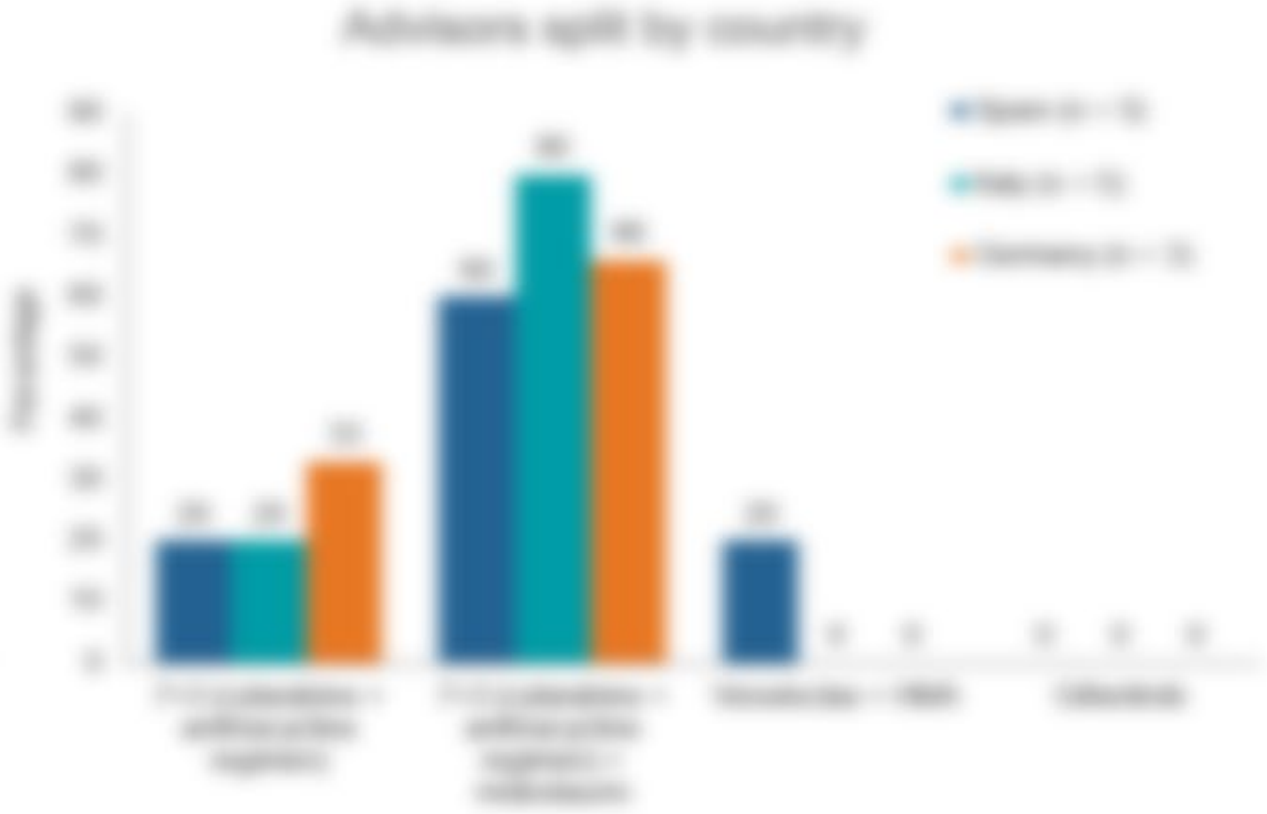
What further steps can be taken to manage the persisting febrile neutropenia? (n = 11*)





*Three advisors did not respond.

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

> Frontline therapy

THE MAJORITY OF ADVISORS WOULD CONSIDER A SECOND COURSE OF THERAPY WITH CPX-351 AND THEN SEND THE PATIENT FOR ALLOGENEIC STEM CELL TRANSPLANT

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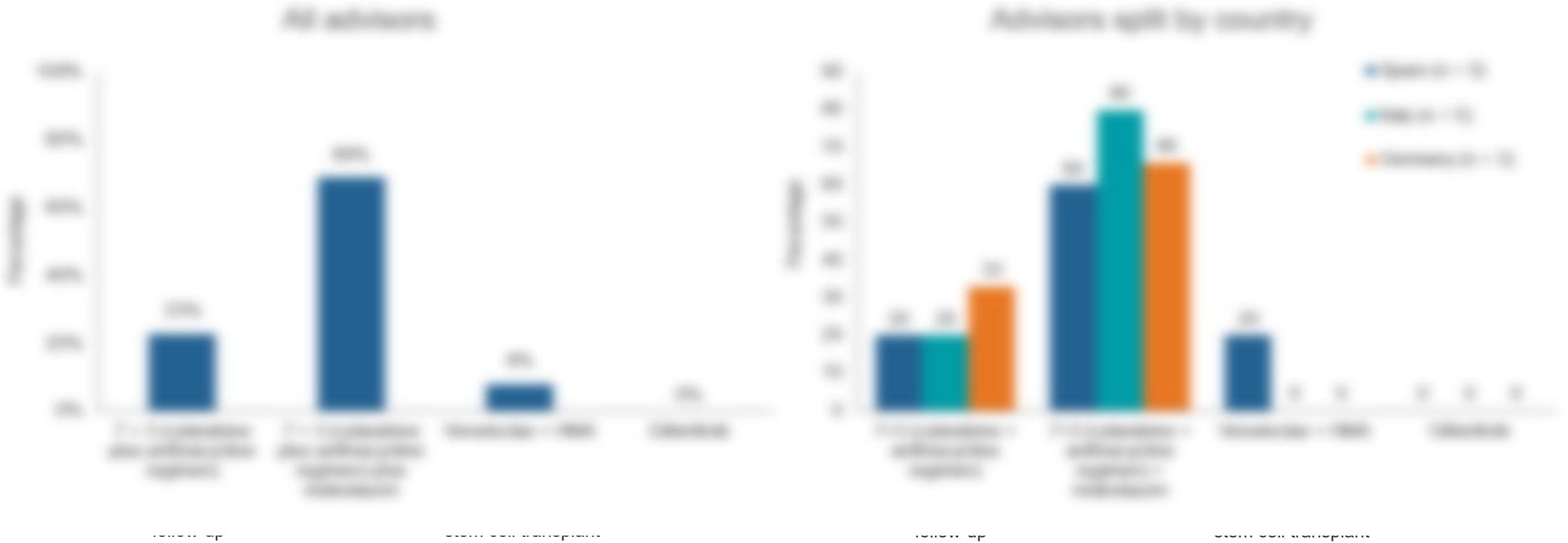
What are the treatment options for this patient? (n = 13*)



*One advisor did not respond.

PATIENT CASE 3: UNFAVORABLE RISK, ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

> Response

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Patient Cases

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO

NEWLY DIAGNOSED AML

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO

CASES

> Patient characteristics

> January 2016

MOST OF THE ADVISORS WOULD REQUEST PCR FOR DRUGGABLE MUTATIONS

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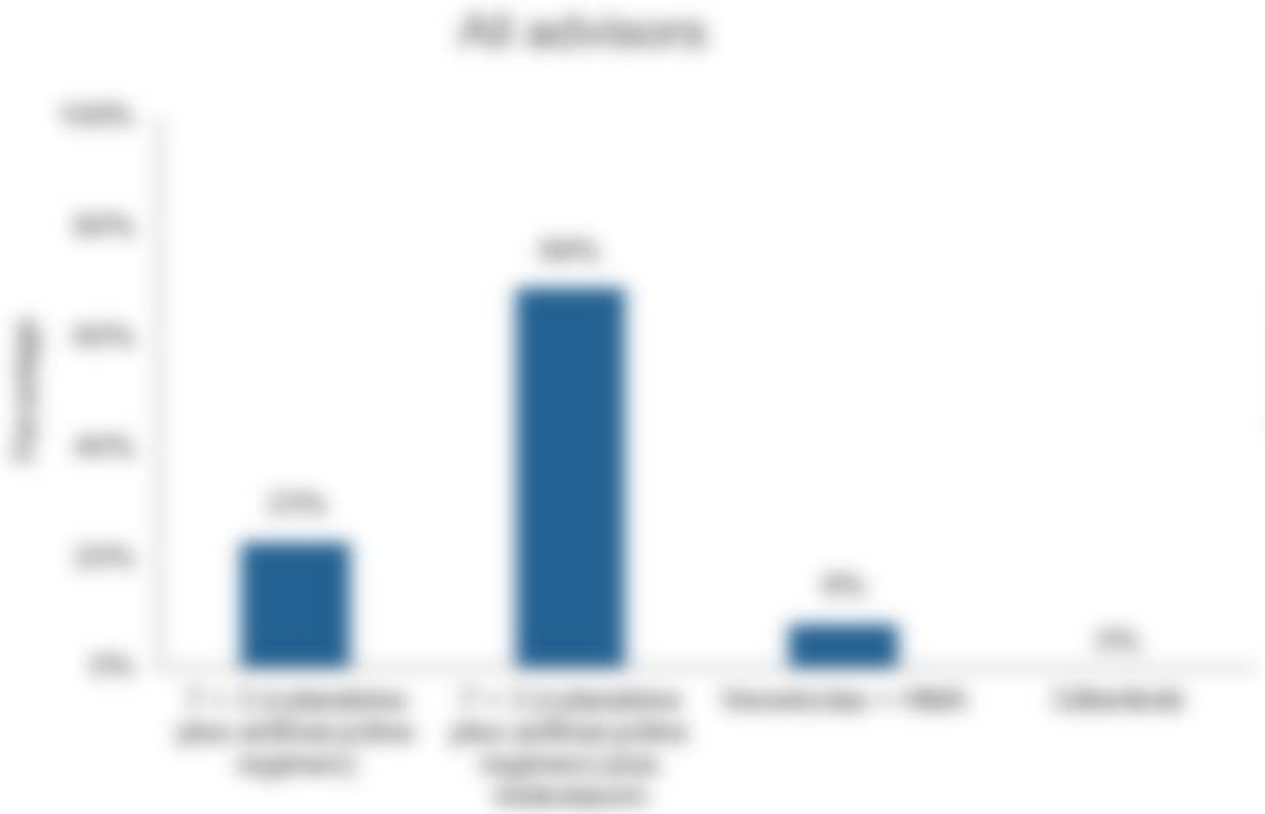
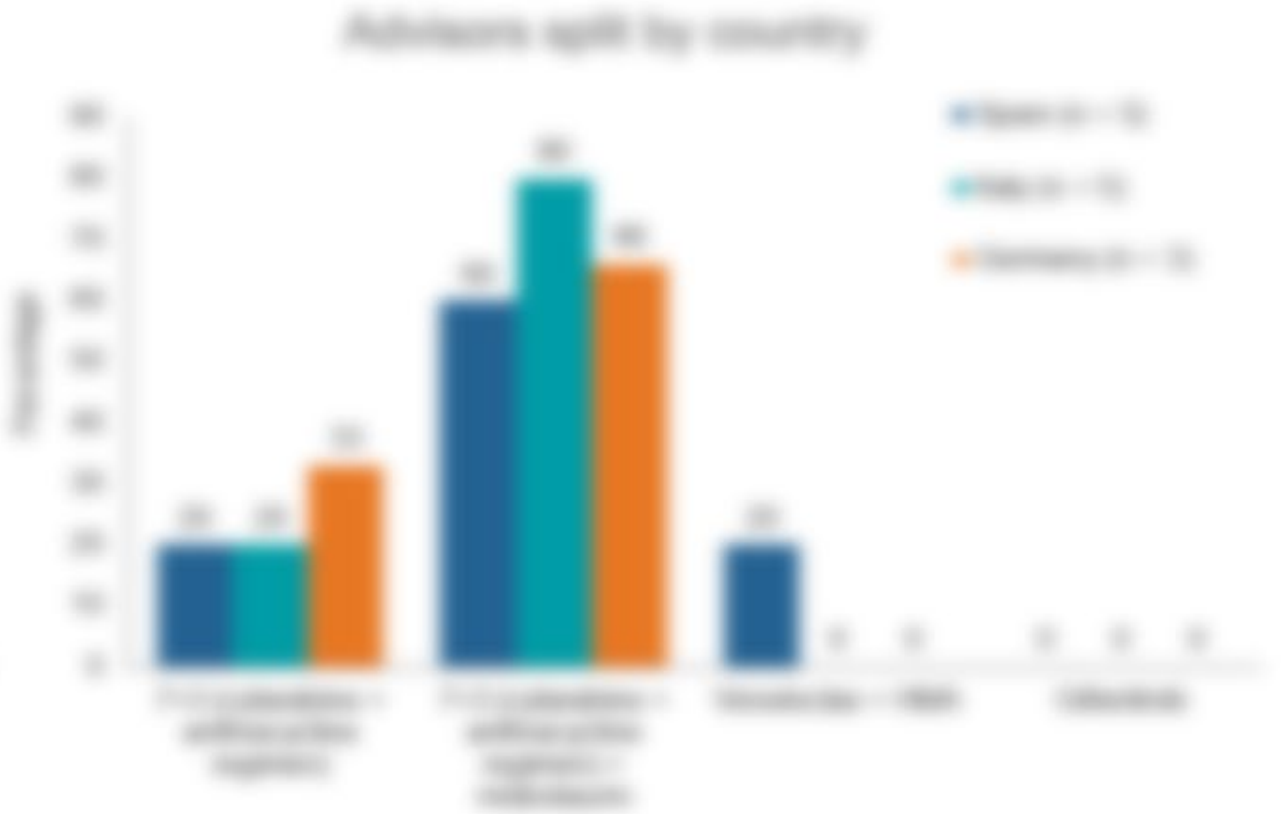
What is the best additional diagnostic workup in such patients? (n = 12*)





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*Two advisors did not respond.

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO, CONT.

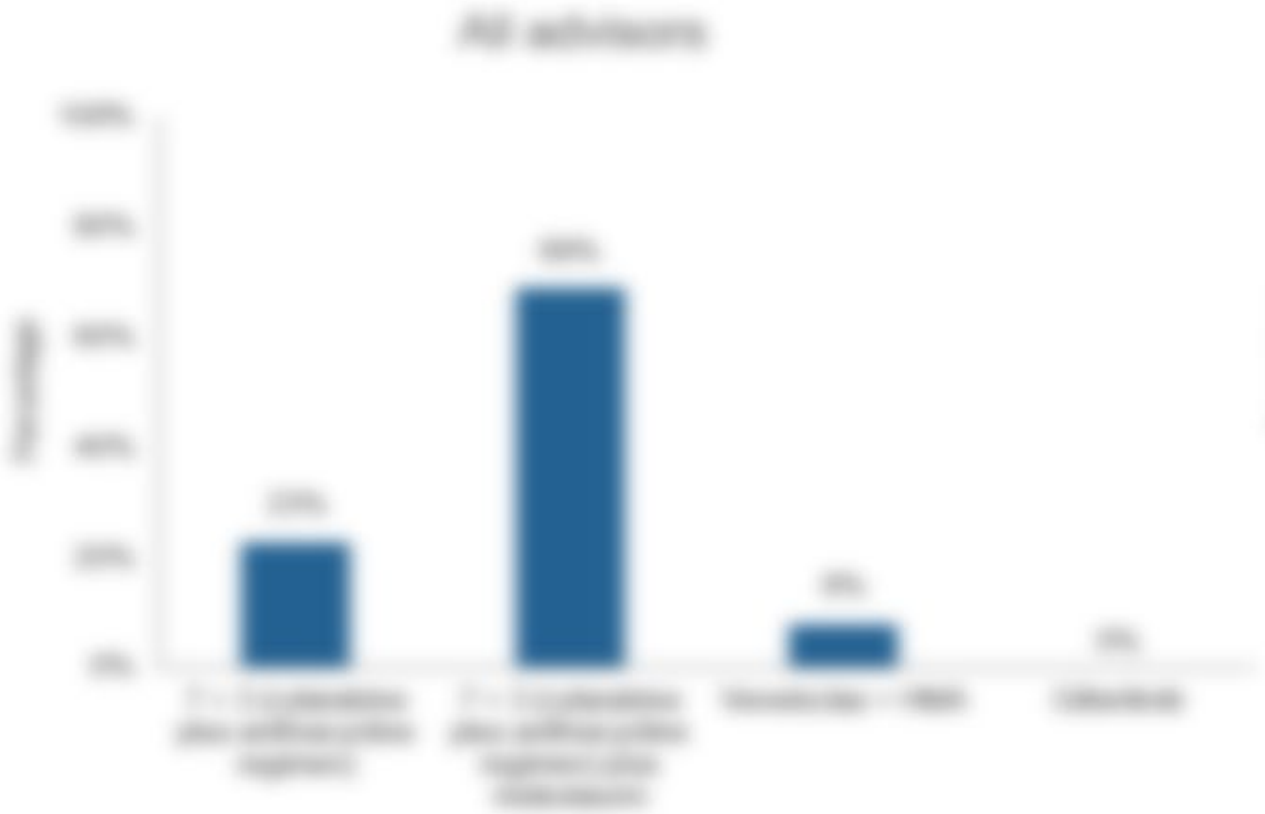
CASES

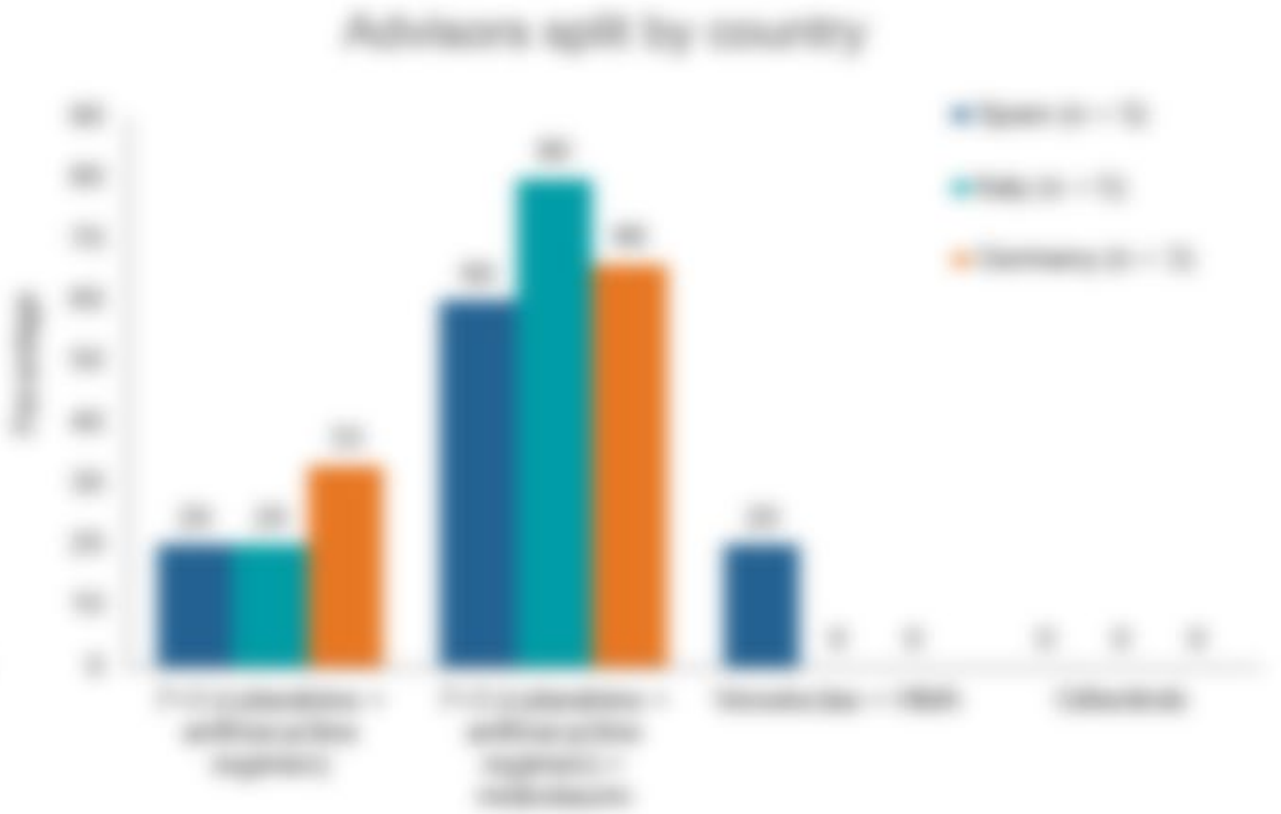
- Diagnostic workup

MOST OF THE ADVISORS WOULD CHOOSE EITHER AZACITIDINE + VENETOCLAX (ALSO AFTER PROGRESSION ON AZACITIDINE) OR A CLINICAL TRIAL AS INDUCTION REGIMEN FOR THIS PATIENT

CASES

What is your preferred induction regimen in such patients? (n = 13*)





*One advisor did not respond.

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

- Induction treatment

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

- Further outpatient management

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO, CONT.

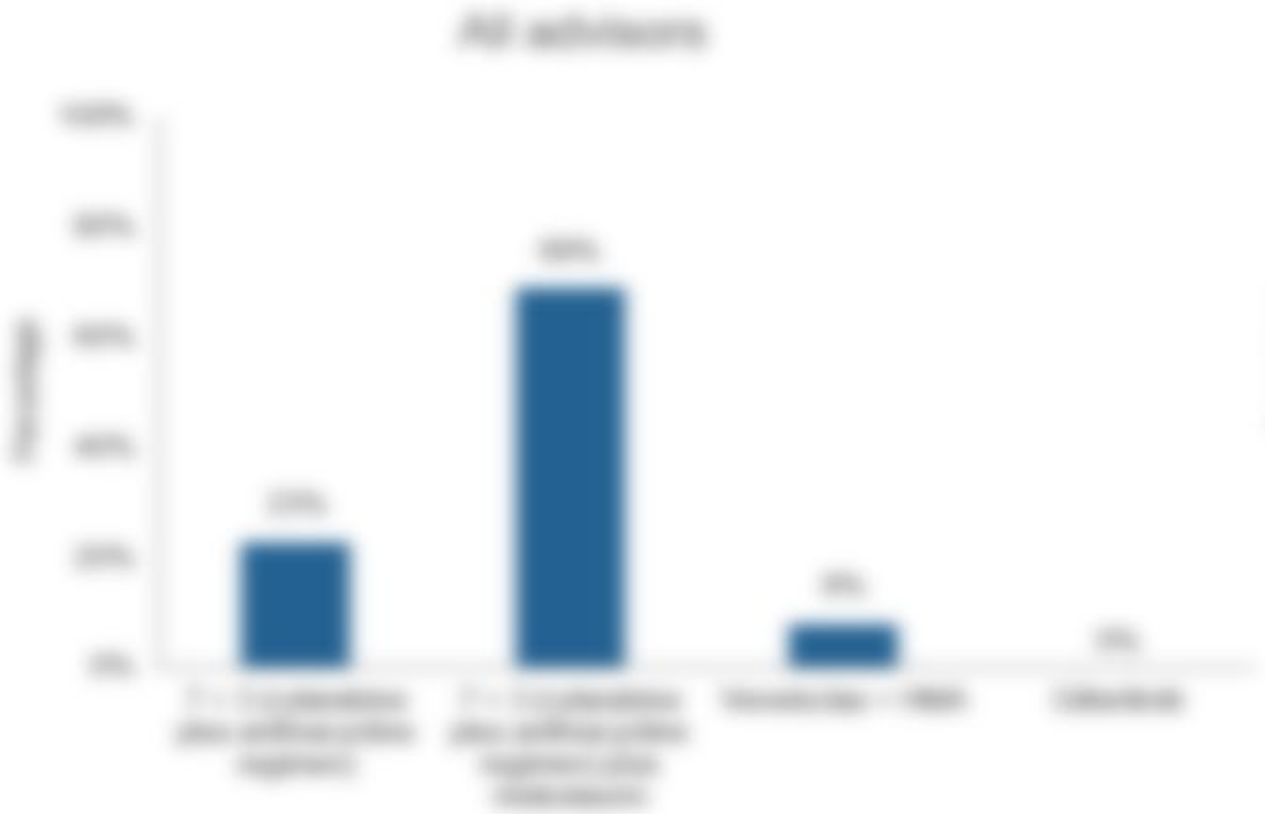
CASES

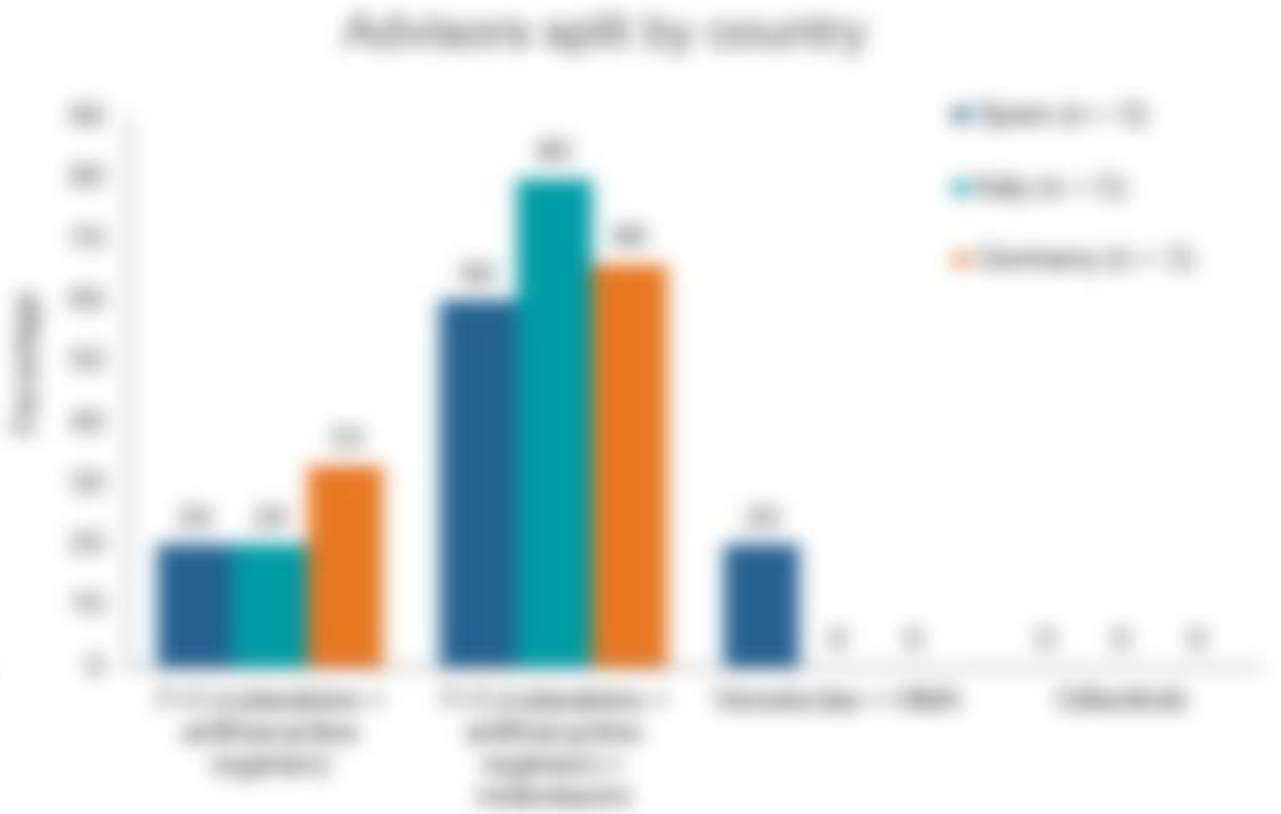
- February 2017: hematologic relapse

MOST OF THE ADVISORS THINK IT IS IMPORTANT TO REPEAT THE MUTATION STATUS FOR THIS PATIENT

CASES

What is false? (n = 7*)





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*Seven advisors did not respond.

PATIENT CASE 4: NO ACTIONABLE MUTATION, NOT ELIGIBLE FOR INTENSIVE CHEMO, CONT.

CASES

- What next?