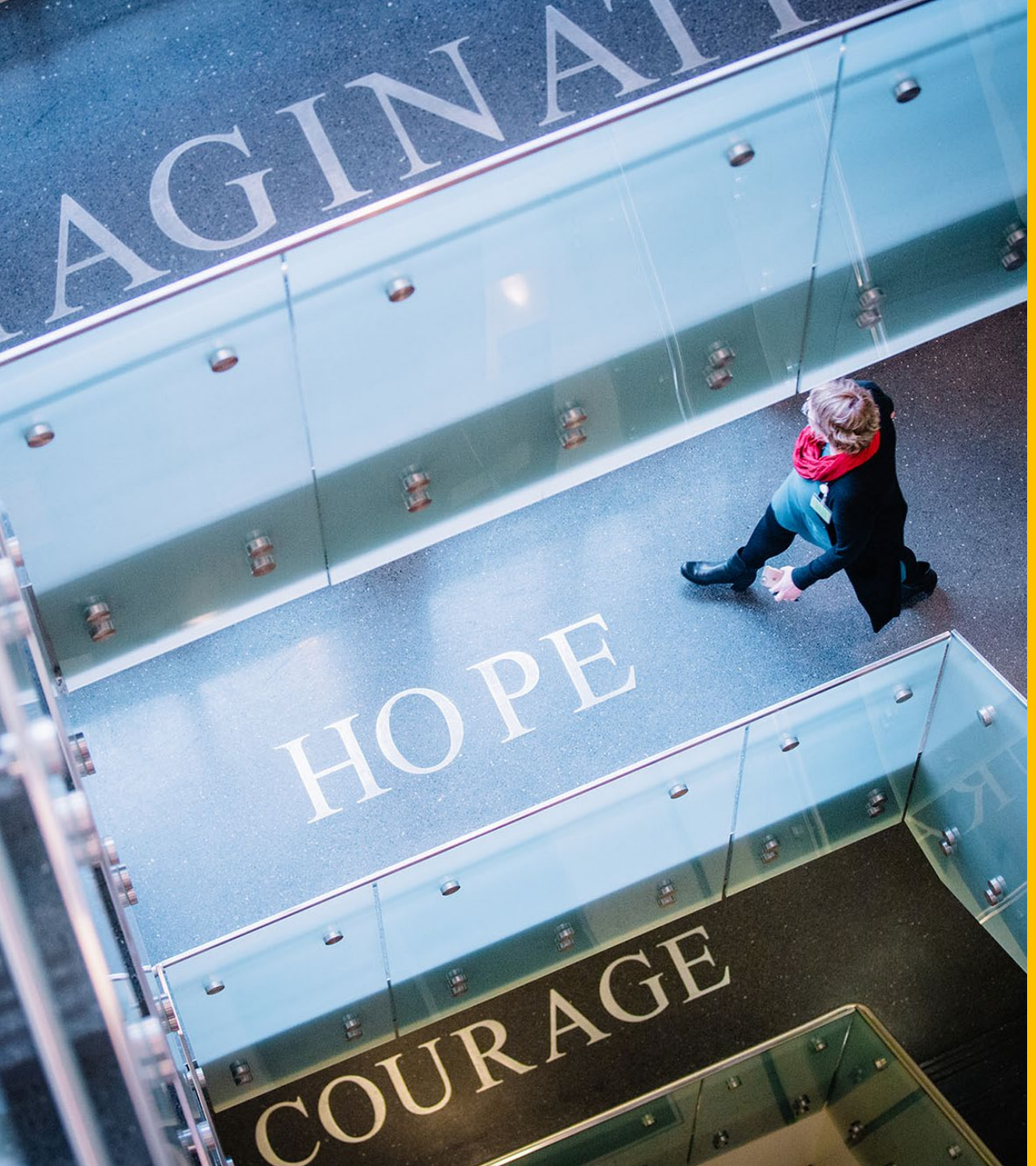

Patient-Based Panel Discussion Leukemia

All Speakers: Drs. Kantarjian, Arellano, Waller, Hunter, Langston, Frank

Case presented by Emory University Heme-Onc fellow: Sarah J. Wood, MD

July 21st, 2023

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute Designated Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

Case Presentation

- Mr. DK is a 73 yo M who was found to have elevated platelets and hemoglobin on a routine CBC in early 2020. Work up was ultimately consistent with polycythemia vera. He was treated with hydroxyurea (500 mg BID) with stabilization of his counts.

- In late 2021, he was admitted to an outside hospital for small bowel obstruction (non-malignant). During this prolonged admission, his hemoglobin and platelet counts continuously declined.

- Hydrea was held, but ultimately was found to have circulating blasts on peripheral smear, prompting transfer of care.

Case Presentation

- On presentation to EUH, pt was vitally stable, physical exam was notable for conjunctival pallor, delayed capillary refill, and scattered ecchymoses. ROS notable for fatigue and easy bruisability of approximately 2-week duration.

- Admission labs as follows:
  - CBC w/ diff: WBC/Hgb/Hct/Plts: **20.9 / 9.6 / 27.9 / 65**
  - **ANC 0, 90% "other cells"**
  - LDH **1094,** Uric Acid 7**,** Ca 9.2, Phos 4. Other chemistries WNL.

- Peripheral flow cytometry was ordered and BMBx performed. Supportive care measures implemented.

Peripheral Blood Flow Cytometry

- Leukocytosis due to numerous circulating blasts comprising >90% of leukocytes on peripheral smear
- Flow cytometry with distinct population comprising 85% of sample and expresses CD7 (dim), CD13, CD33 (dim), CD34, CD56 (dim), CD117, CD123 (dim), HLA-DR, and CD45
- AML FISH panel: negative

Taken together, results demonstrate presence of phenotypically distinct population of myeloblasts, consistent with Acute Myelogenous Leukemia

Bone Marrow

- BMBx
  - Blasts account for ~60% of total cells and display myeloid differentiation by flow cytometric analysis (same immunophenotype as peripheral flow)
  - “The patient’s history of polycythemia vera is noted and the disease is **best classified as secondary AML**”
  - Cytogenetics: Normal
  - FISH AML: Negative
  - Myeloid Mutation Panel 75 (MMP-75)
    - ASXL1 c.1537G>T: detected in approximately 47% of alleles
    - IDH1 c.394C>T: detected in approximately 47% of alleles
    - JAK2 c.1849G>T: detected in approximately 95% of alleles
    - SRSF2.c284C>A: detected in approximately 48% of alleles

Case Presentation

- Given diagnosis of transformed AML (t-AML), pt began induction chemotherapy with liposomal cytarabine-daunorubicin in December 2021
- Beginning in January 2022, his WBC and Hgb had stabilized, but platelets increased rapidly to 2 million per microliter, suggesting conversion back to myeloproliferative state. After a long discussion regarding therapeutic options, it was decided to reinitiate hydroxyurea. Ruxolitinib was considered, but too cost-prohibitive
- He was maintained on hydroxyurea monotherapy with normalization of counts until June 2022 when leukopenia and neutropenia ensued…

Case Presentation

- When counts began to decline, hydroxyurea urea was held, however ultimately circulating blasts (65% on peripheral flow) were identified, thus affirming reversion back into overt AML
- Given IDH1 mutation (and lack of transplant candidacy), Mr. DK was started on the IDH inhibitor ivosidenib in August ~2022 with clinical and laboratory improvement.
- Over the next few months, his WBC count again began to rise reaching 160k. He was then resumed back on hydroxyurea.
- **To date, Mr. DK remains on ivosidenib plus hydroxyurea 500 mg daily with essentially normal counts.**

Panel Case Discussion, Q&A

- This is an interesting and illustrative case of an MPN that converted to AML (post-MPN AML), then converted back to an MPN state.

- Now, seemingly, both diseases are being controlled with targeted therapy (IDH inhibitor) plus cytoreduction(hydroxyurea).

- Can you discuss some of the specific challenges about this case, such as how you approached his initial conversion back to myeloproliferative state and decision to resume hydroxyurea? What are your key take-aways?

Thank you