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BACKGROUND

- Acute promyelocytic leukemia (APL) accounts for 5% of adult AML cases with approximately 1,000 cases per year in the United States.
- The overall survival of low/intermediate risk APL with ATRA/ATO regimen exceeded 95% in the pivotal APL0406 trial.
- Early deaths, typically within 30 days of presentation, have constituted around 20-30% in real world data.
- Catastrophic bleeding, differentiation syndrome, and infection remain the most common causes of early mortality in patients with APL.
- Current practices, as based on NCCN 2020 and ELN 2019 guidelines, recommend bone marrow biopsy (BMBx) at the end of induction (EOI) course to document morphologic remission.
- However, given the virtual absence of disease resistance and frequently misleading cytomorphologic features due to delayed blast differentiation, the indication for EOI BMBx has recently come into question.
- Little is known about the outcomes with a fixed duration induction course and little data exists to support the requirement of EOI BMBx.

OBJECTIVE

- To assess the utility of end of induction bone marrow biopsy morphologic findings in APL patients treated with 28-day ATRA/ATO induction regimen.

METHODS

- A retrospective study was performed from patients treated at the University of Alabama at Birmingham from 12/2012 to 3/2020.
- Patients ≥ 18 years of age treated for APL with ATRA/ATO ± cytoreductive agent were included. Those who received >30 doses of ATO or those who died in first 4 weeks were excluded.
- Demographics, hematologic parameters, treatment details, and BMBx results were collected. Time-to-event endpoints were calculated from day 1 of ATO.

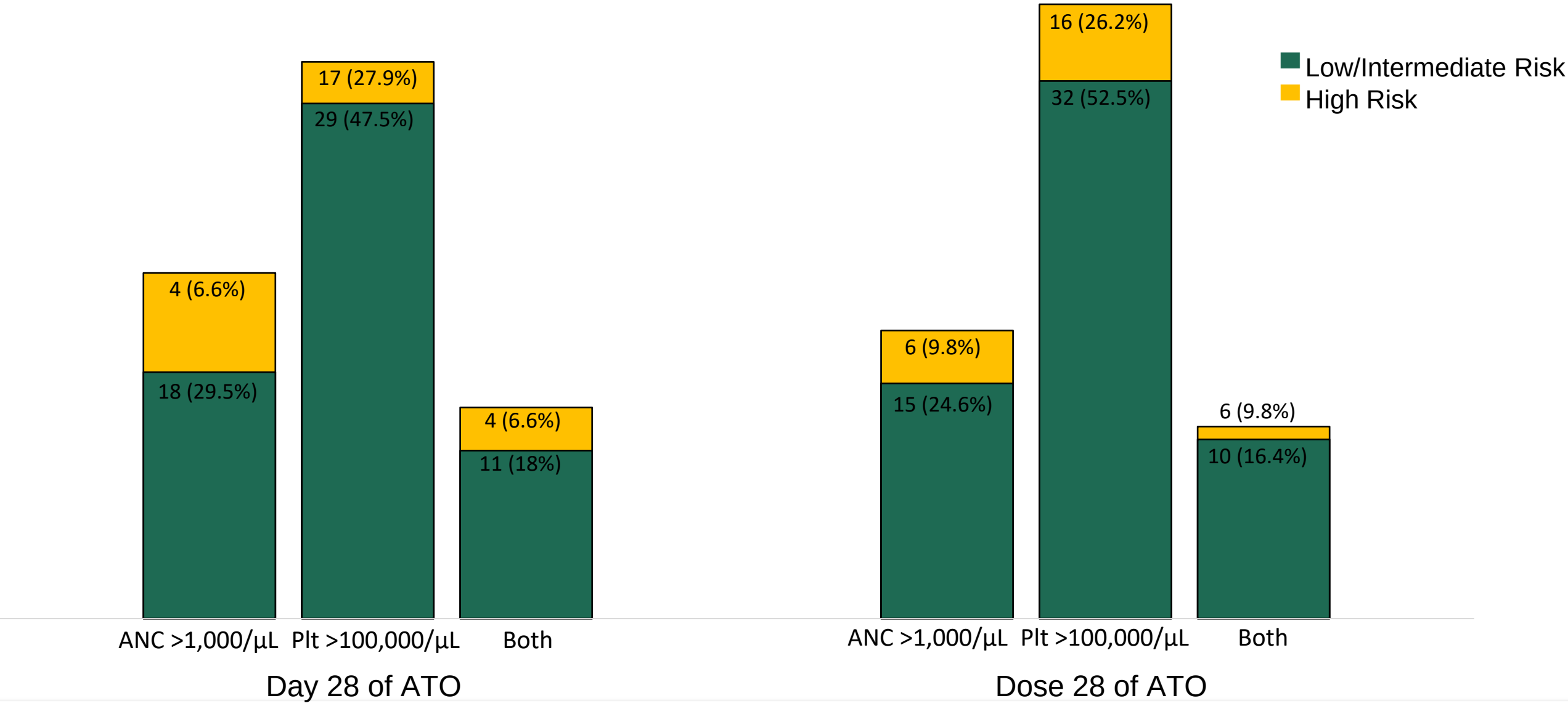
RESULTS

Table 1. Patient characteristics

|                        | All<br>(N = 61) | Low or Intermediate Risk<br>(N = 42) | High Risk<br>(N = 19) |
|------------------------|-----------------|--------------------------------------|-----------------------|
| Age – years            |                 |                                      |                       |
| Median                 | 51              | 49                                   | 51                    |
| Range                  | 21-81           | 21-81                                | 25-76                 |
| Sex – number (%)       |                 |                                      |                       |
| Male                   | 34 (55.7%)      | 25 (59.5%)                           | 9 (47.4%)             |
| Female                 | 27 (44.3%)      | 17 (40.5%)                           | 10 (52.6%)            |
| Race – number (%)      |                 |                                      |                       |
| White                  | 47 (77.1%)      | 33 (78.6%)                           | 14 (73.7%)            |
| Black                  | 13 (21.3%)      | 8 (19%)                              | 5 (26.3%)             |
| Other                  | 1 (1.6%)        | 1 (2.4%)                             | 0 (0%)                |
| WBC at Presentation    |                 |                                      |                       |
| Median                 | 2.89            | 1.5                                  | 30.11                 |
| Range                  | 0.46-153.88     | 0.46-8.63                            | 13.03-153.88          |
| Plt at Presentation    |                 |                                      |                       |
| Median                 | 27.1            | 29.75                                | 23.2                  |
| Range                  | 7.1-181.1       | 7.1-181.1                            | 7.1-80.5              |
| Received Anthracycline | 12 (19.7%)      | 2 (3.3%)                             | 10 (16.4%)            |
| Received GO            | 5 (8.2%)        | 0 (0%)                               | 5 (8.2%)              |

- Median time to dose 28 ± 2 of ATO was 28 days (range 27-40).
- Day 28 hematologic parameters showed that 22 (36%) patients had an ANC > 1,000/μL, 46 (75.4%) had platelets > 100,000/μL, and 15 (24.5%) had both. Mean ANC was 1,250/μL and platelets 238,700 /μL.
- On the day of ATO dose 28 ± 2, 21 (34.4%) patients had an ANC > 1,000/μL, 48 (78.7%) had platelets > 100,000/μL, and 16 (26.2%) had both. Mean ANC was 1,130/μL and platelets 247,200/μL. Neither was significantly different from cell counts on day 28 of ATO (p=0.668 and p=0.794).
- ANC (780/μL vs. 1,550/μL; p=0.03) and platelets (180/μL vs. 247/μL; p=0.56) were higher for patients who received GO or anthracycline as compared to those who did not.

Figure 1. Number of patients who achieved hematologic remission at D28 of ATO vs day of dose 28 of ATO.



RESULTS (CONT.)

- 51 patients underwent EOI BMBx.
- The median time to EOI BMBx was 43 days (32-59 days) as calculated from day 1 of ATO administration.
- 49 (96%) of these showed no morphologic evidence of APL. The remaining two (4%) were equivocal.

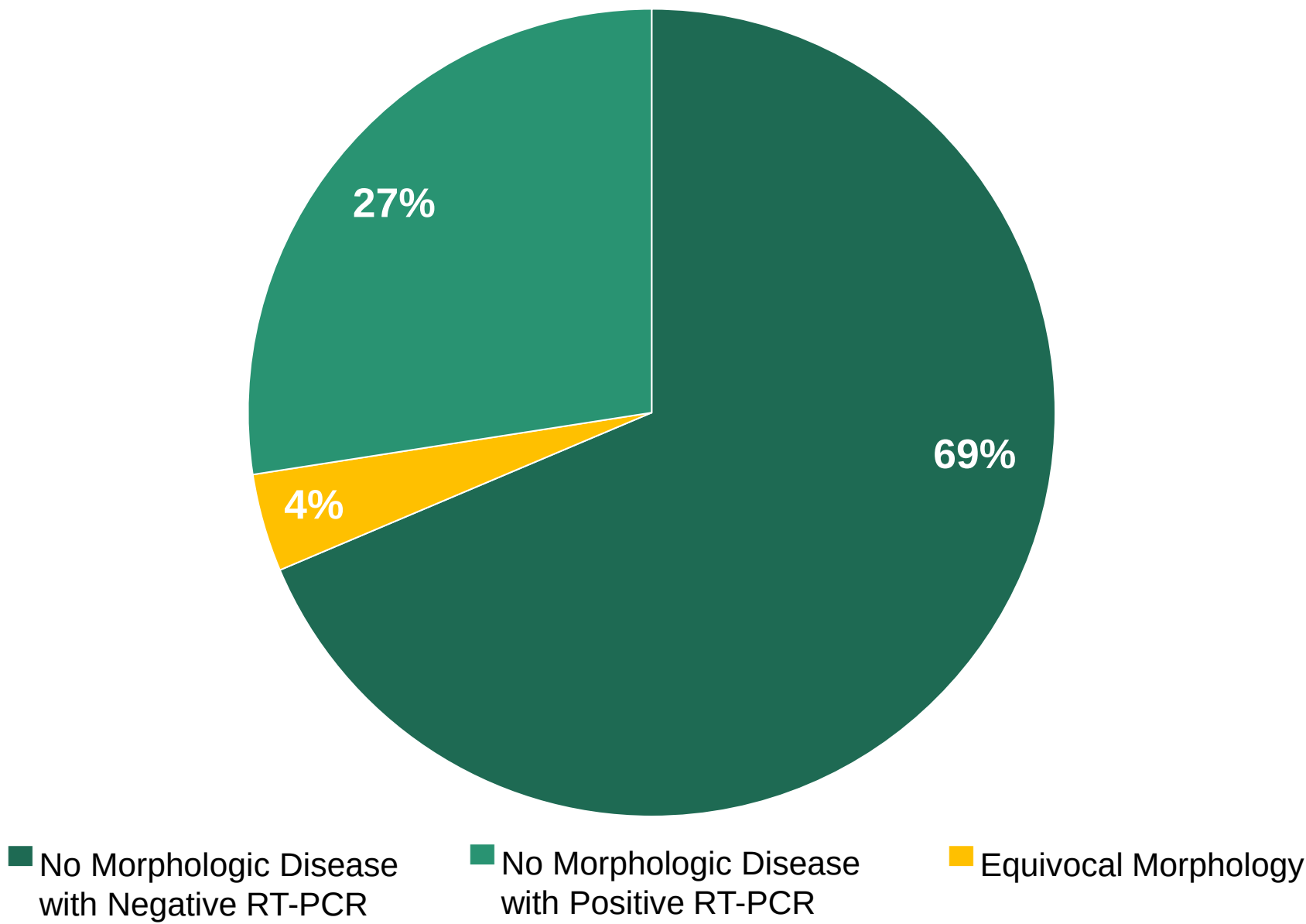


Figure 2. Results of EOI BMBx.

KEY OUTCOMES AND DISCUSSION

- After a median follow-up of 672 days, overall survival was 95% within the study population. Two patients died secondary to complications of APL following EOI. One died from septic shock during consolidation.
- No patients relapsed.
- A 28-dose ATO containing ATRA/ATO regimen delivers excellent outcomes.
- An EOI BMBx may be safely omitted irrespective of hematologic parameters.
- Further data collection, ideally from additional institutions, is necessary to attain larger sample size and validate these findings.

REFERENCES

Lo-Coco F, Avvisati G, Vignetti M, et al. Retinoic acid and arsenic trioxide for acute promyelocytic leukemia. *N Engl J Med*. 2013;369(2):111-121.

Sanz MA, Fenaux P, Tallman MS, et al. Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. *Blood*. 2019;133(15):1630-1643.

National Comprehensive Cancer Network. Acute Myeloid Leukemia (Version 3.2021). [http://www.nccn.org/professionals/physician\\_gls/pdf/aml.pdf](http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf).

Miller KP, Venkataraman G, Gocke CD, et al. Bone Marrow Findings in Patients With Acute Promyelocytic Leukemia Treated With Arsenic Trioxide. *Am J Clin Pathol*. 2019;152(5):675-685.