

Case SH2017-0068

Yahya Al-Ghamdi, Brett Mahon,
Jamile Shammo, Ira Miller



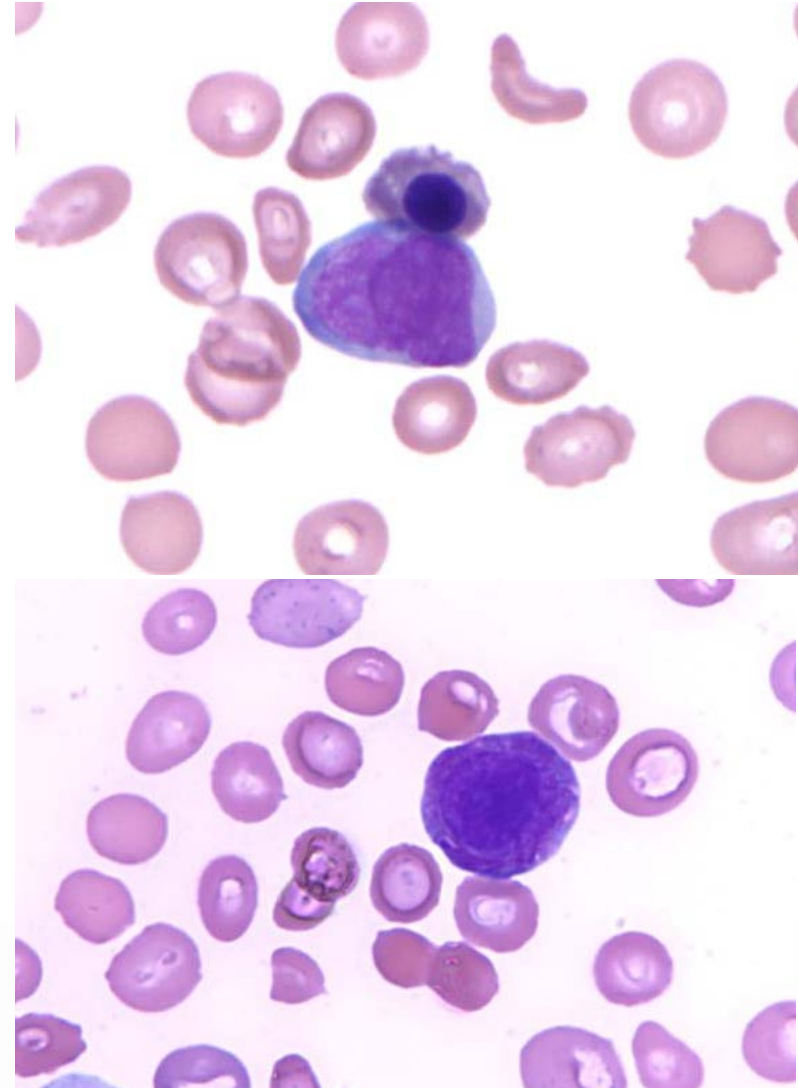
- Nothing to disclose

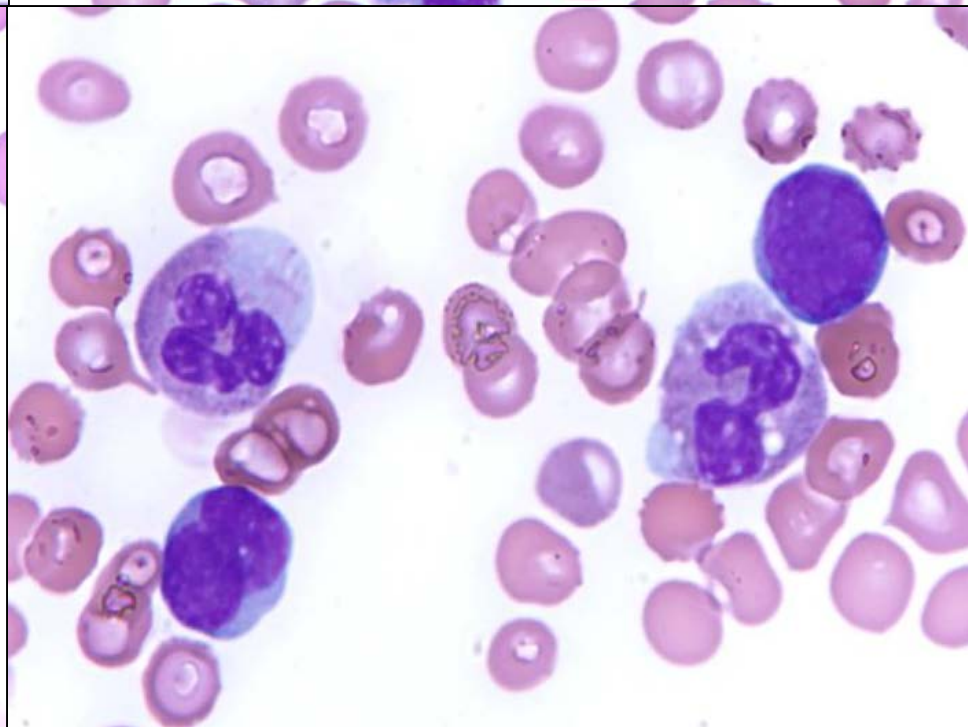
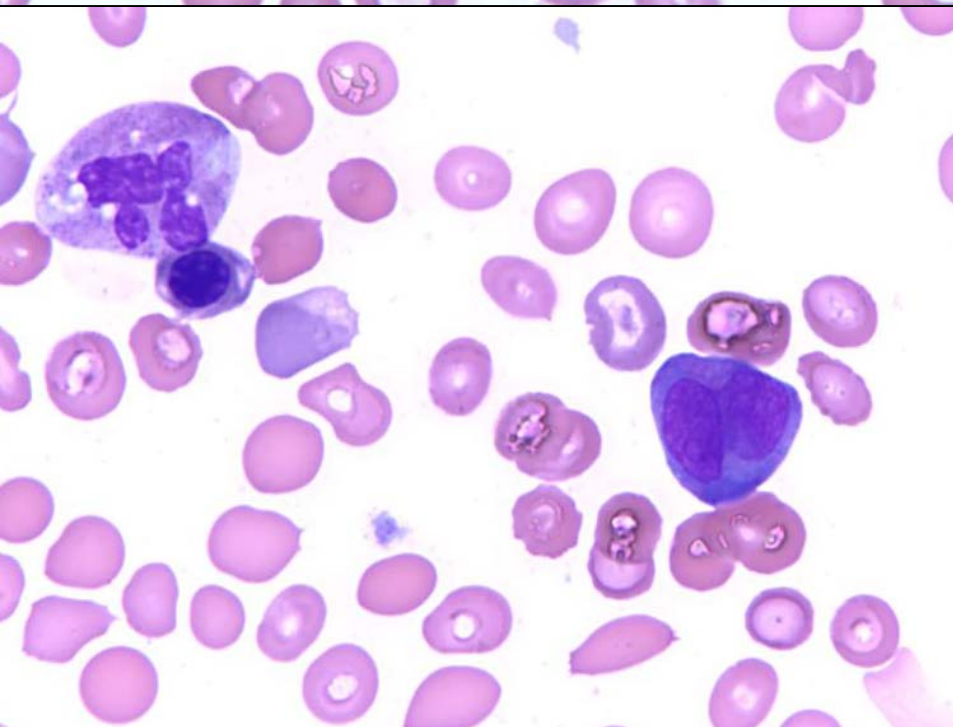
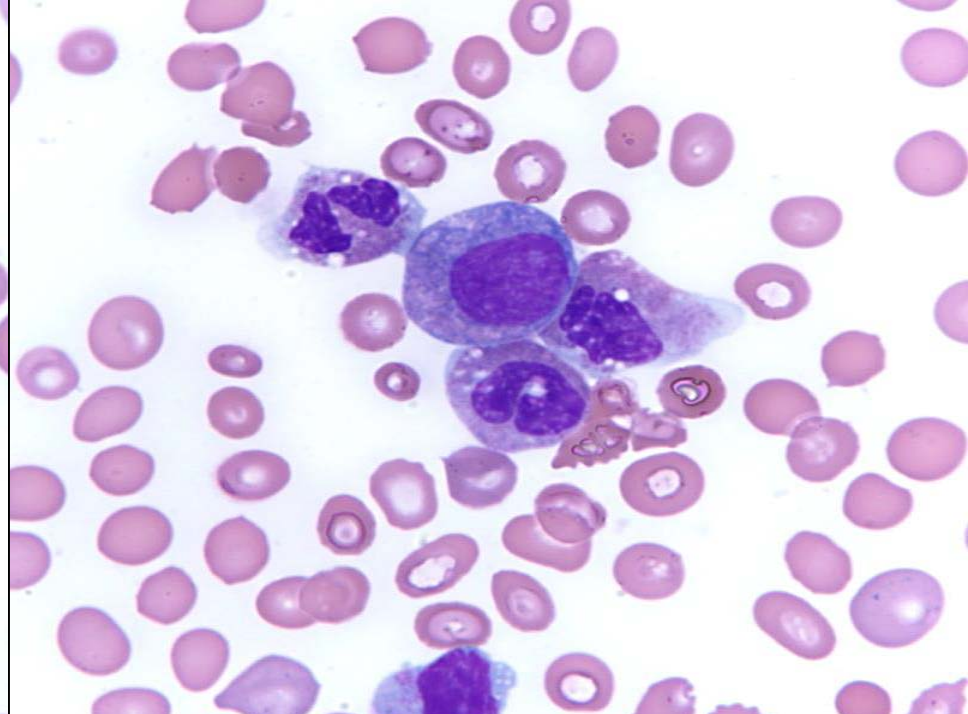
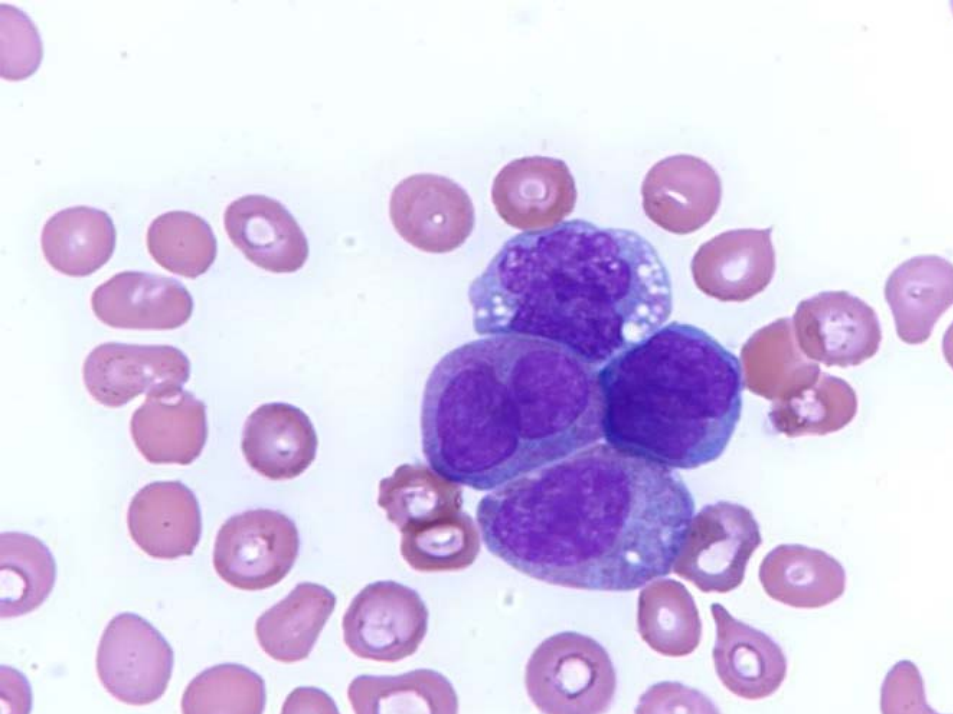
Clinical History

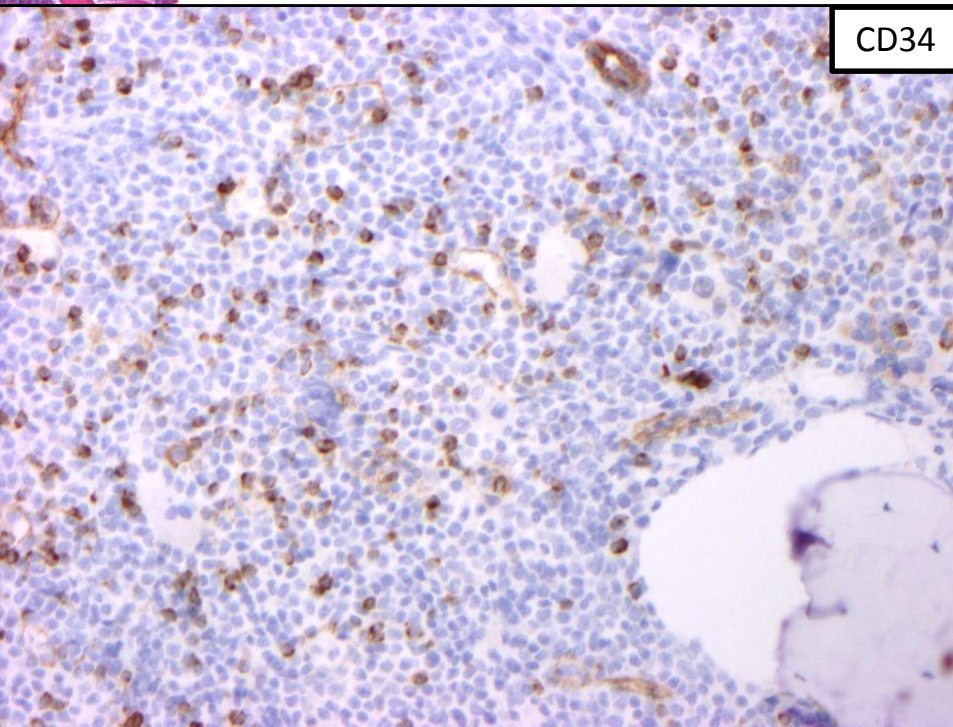
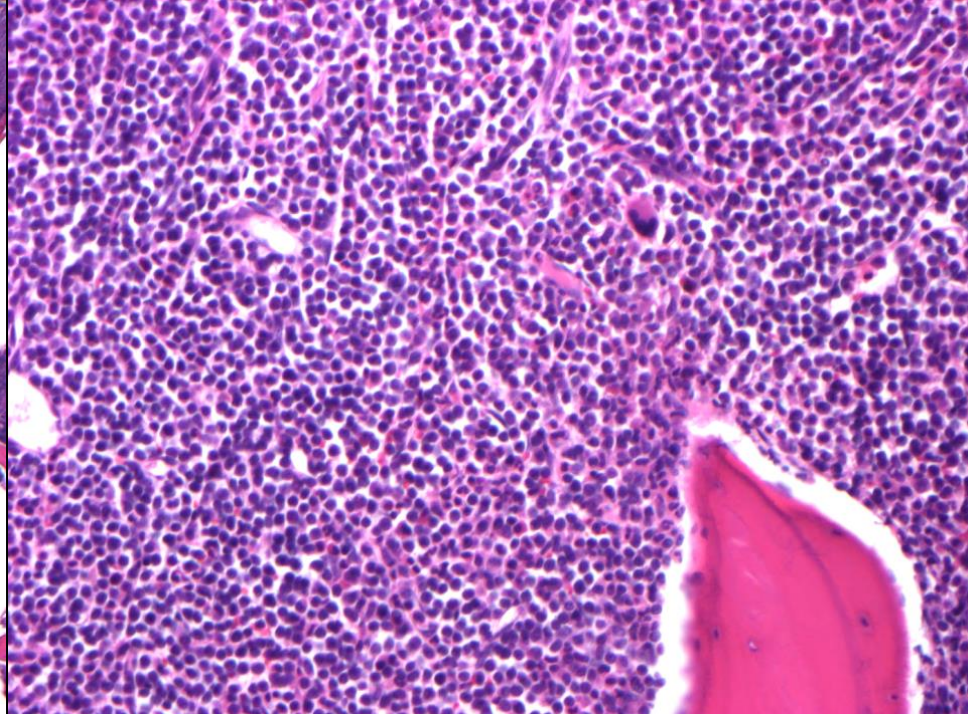
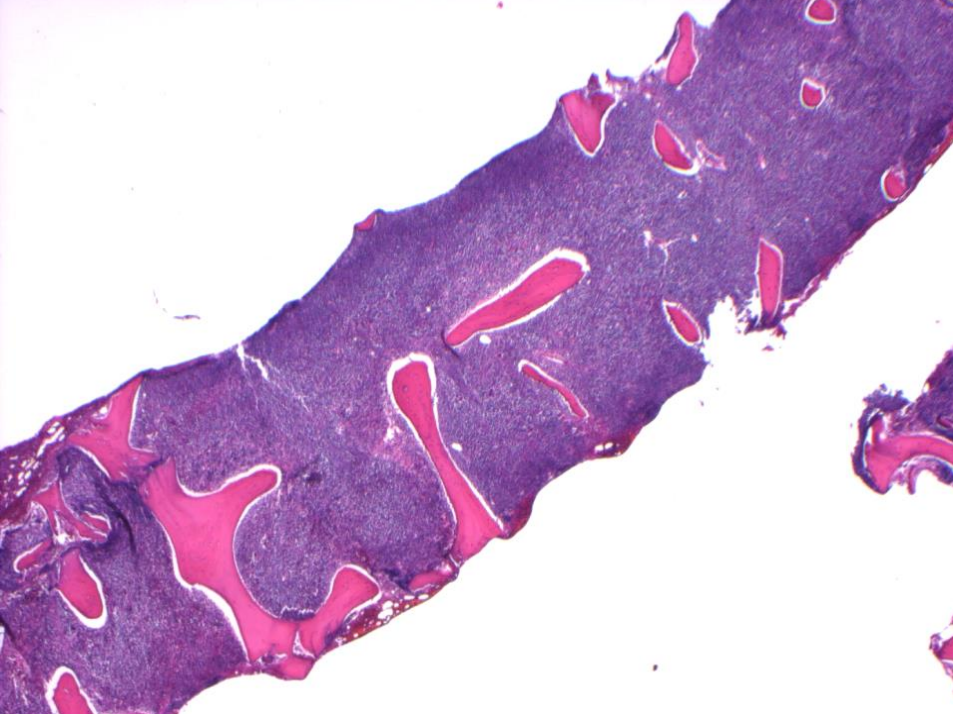
- A 46 year-old male with CML for 3 years presented with abdominal pain and laboratory findings concerning for blast crisis
- PMH:
 - The patient had been in chronic phase for 3 years
 - BCR-ABL+
 - Initially was treated with nilotinib; complicated by pancreatitis
 - Switched to imatinib; no hematologic response
 - Non compliant; ultimately switched to dasatinib

Peripheral Blood

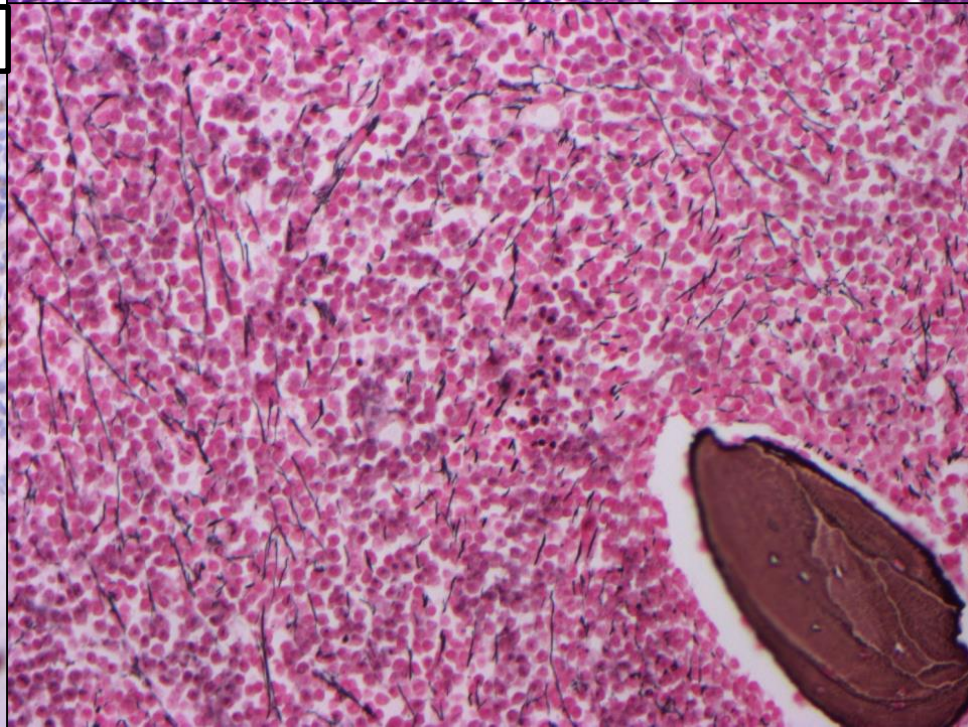
- **WBC: 88.47 th/ μ L (H)**
- **ANC: 18.99 th/ μ L (H)**
- **HGB: 7.8 g/dL (L)**
- **PLT: 65 th/ μ L (L)**

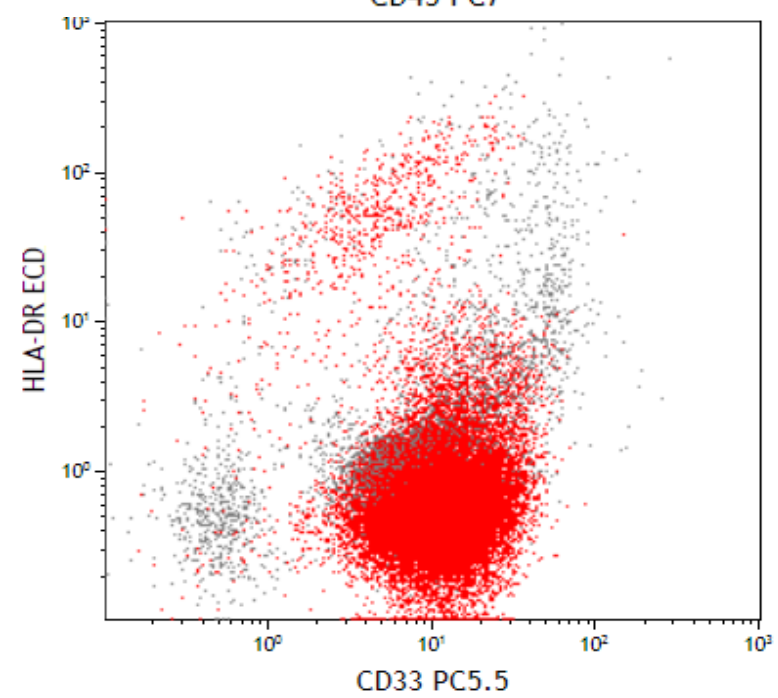
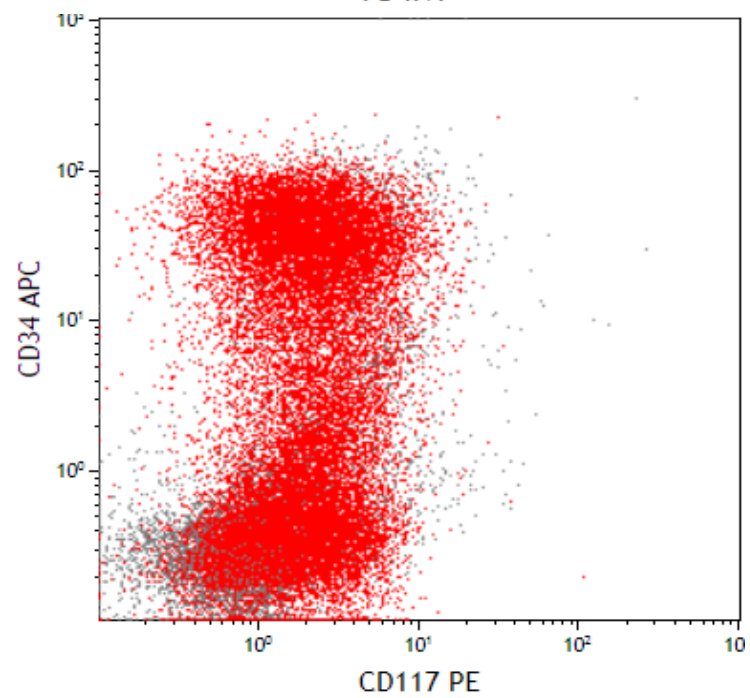
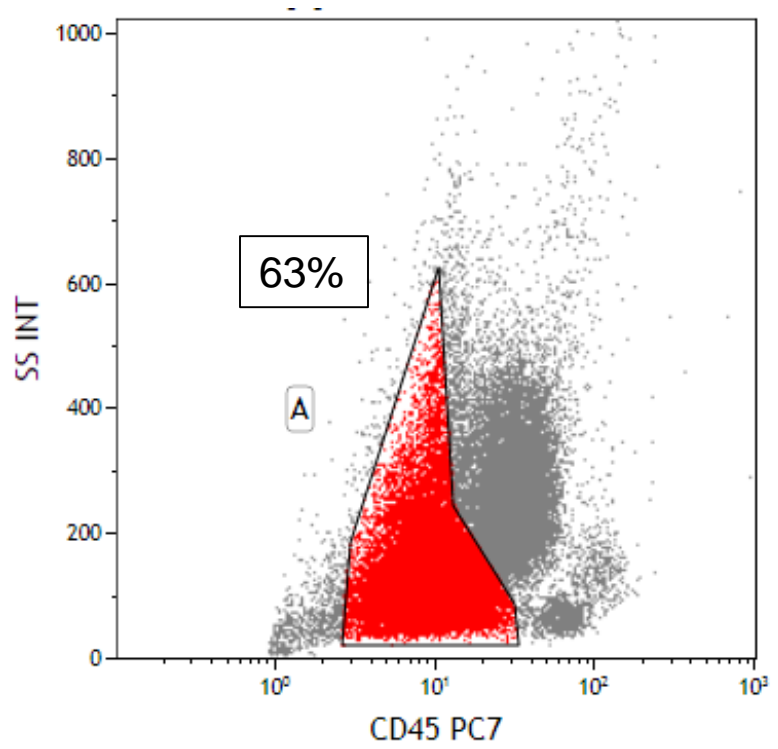
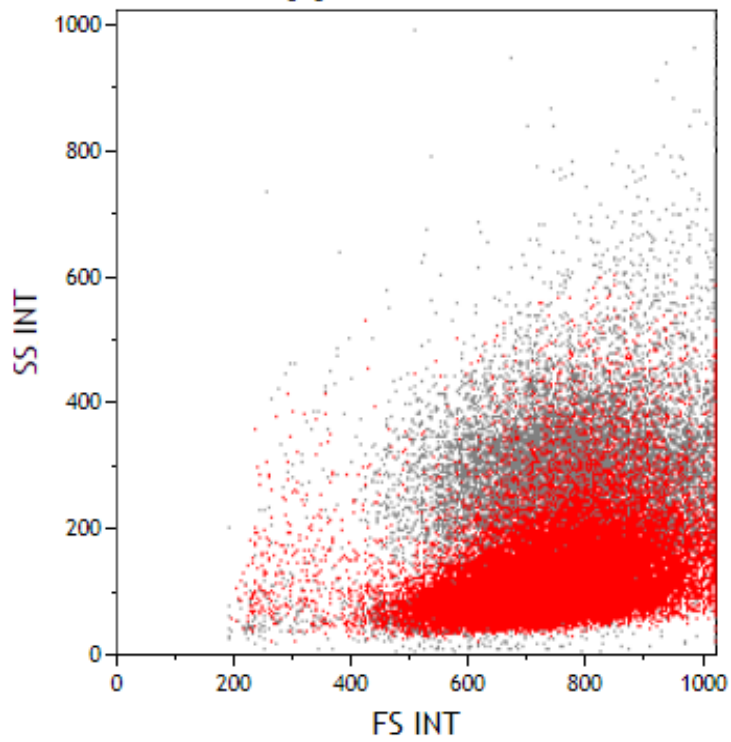


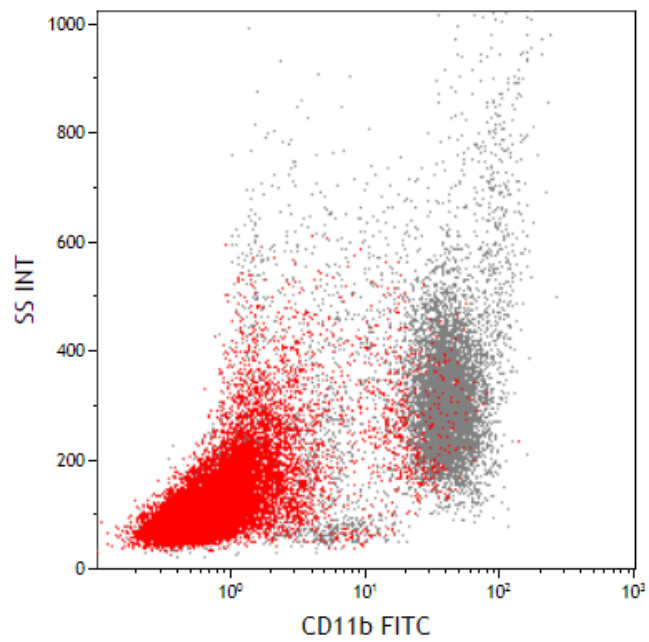
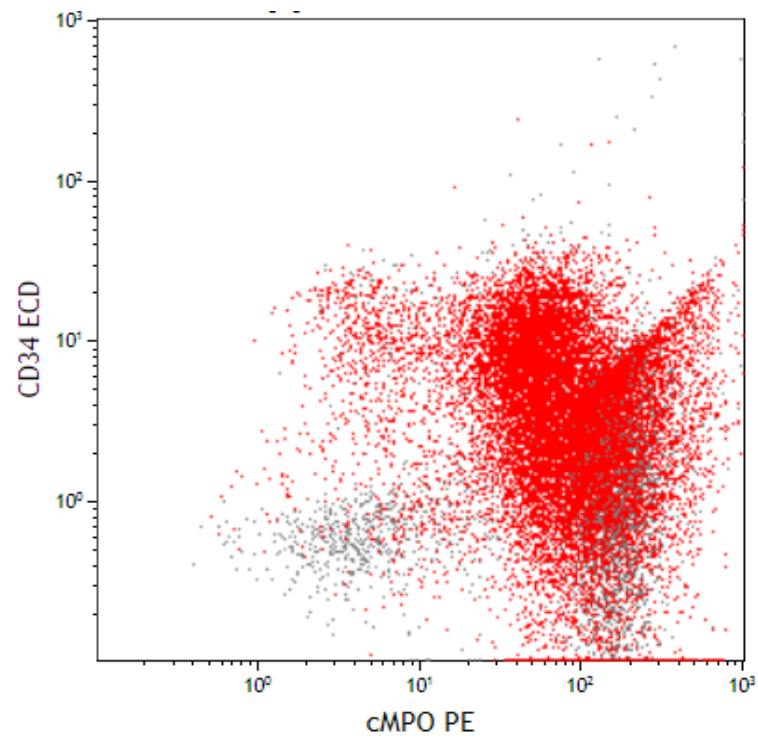
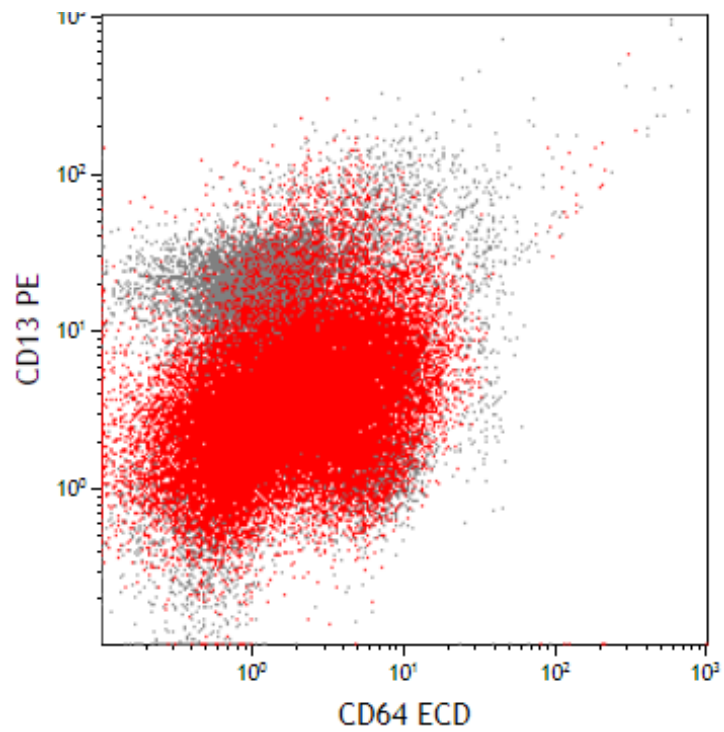




CD34





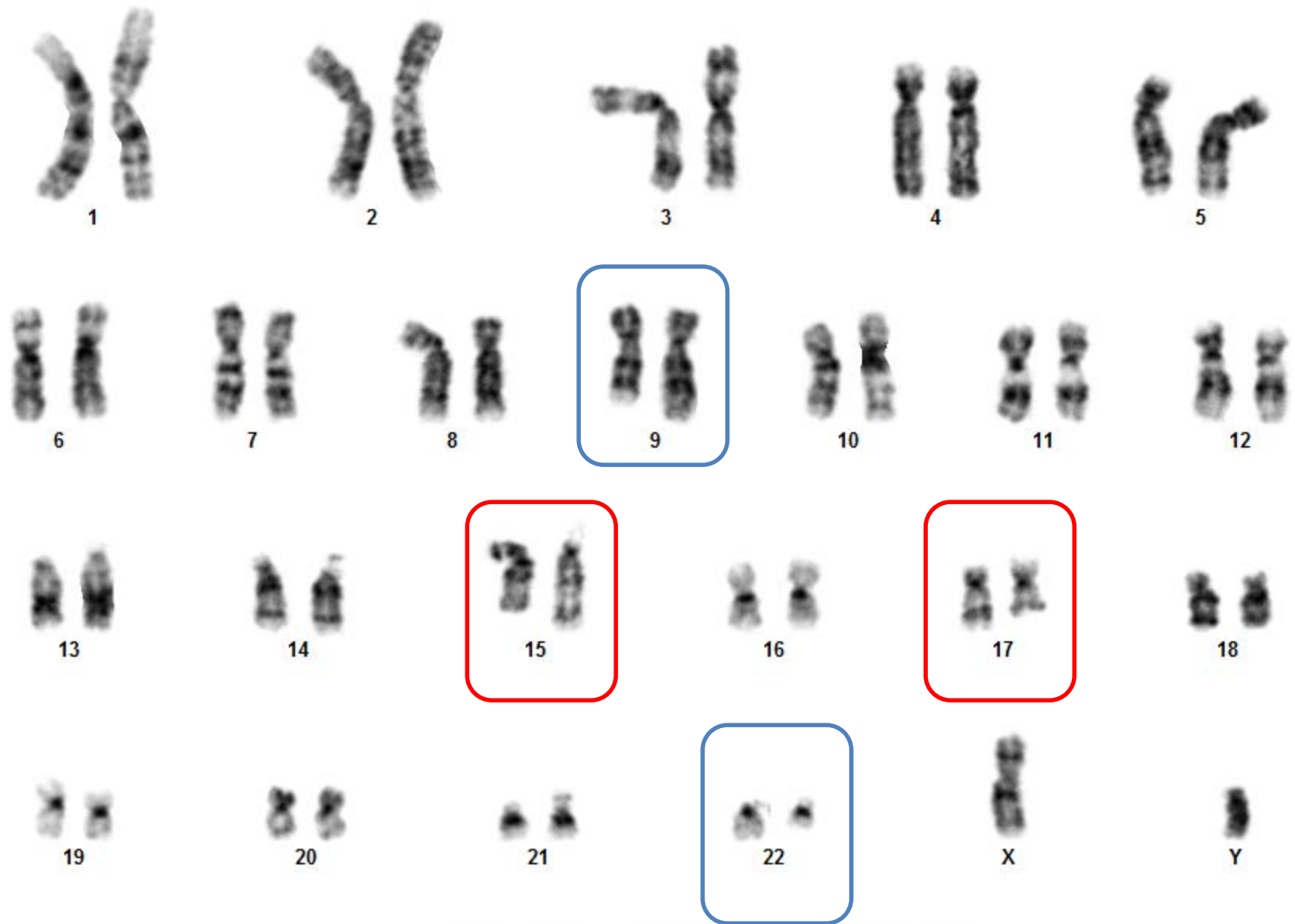


Preliminary Diagnosis

- Chronic myeloid leukemia, blast phase (myeloid)

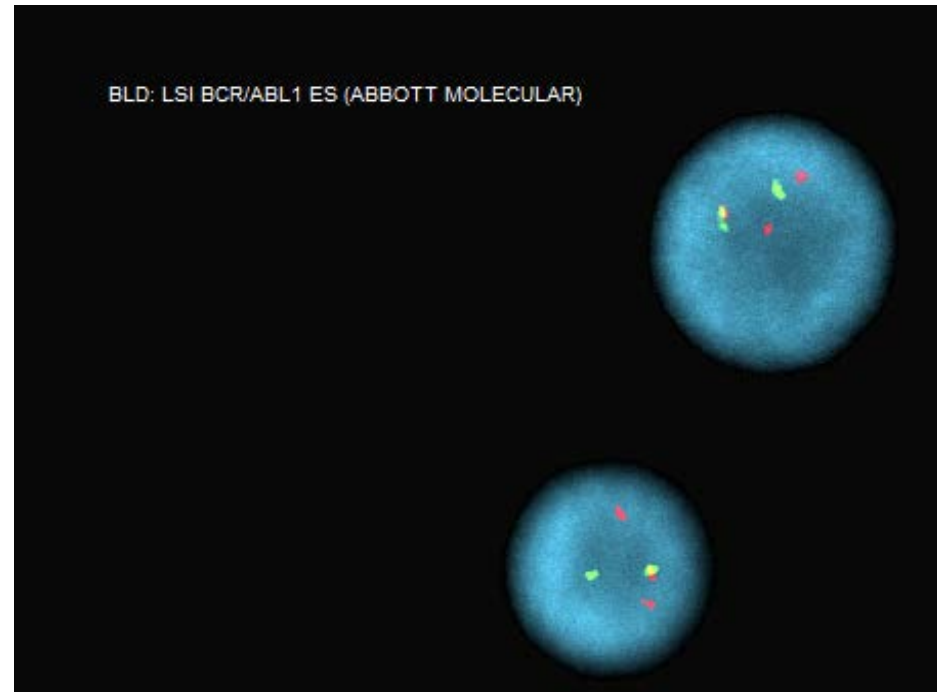
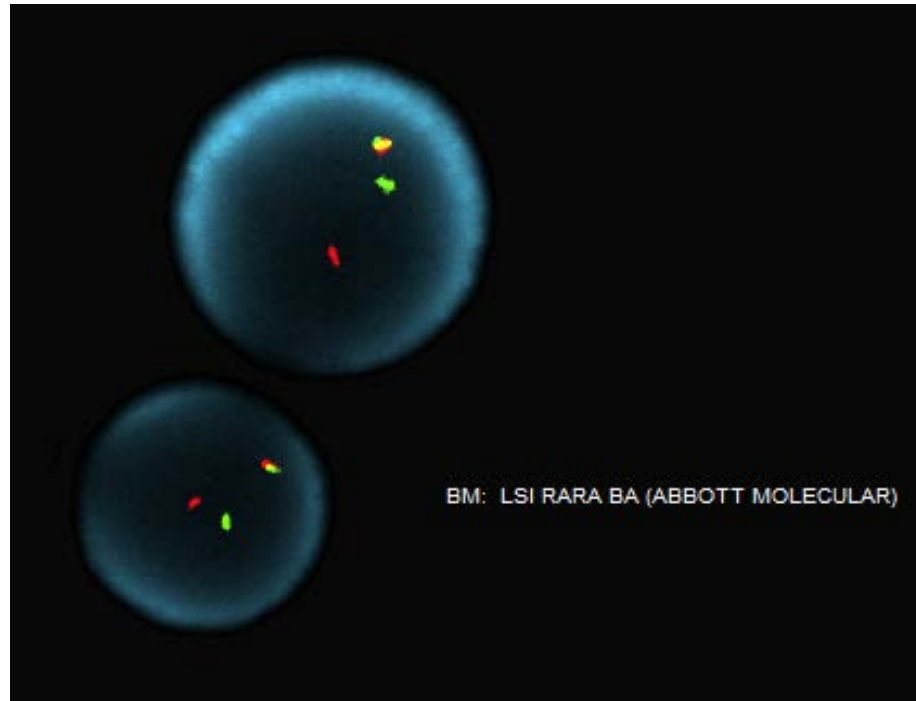
Clinical Course

- The patient received induction chemotherapy with high dose cytarabine and mitoxantrone
- Day 13 BMBx: Marked hypocellular marrow (5%) with fibrosis and scattered maturing granulocytes and occasional atypical immature cells



Blood(spec): 46,XY,t(9;22),t(15;17)

FISH: Positive for RARA and BCR-ABL gene rearrangements



Final Diagnosis

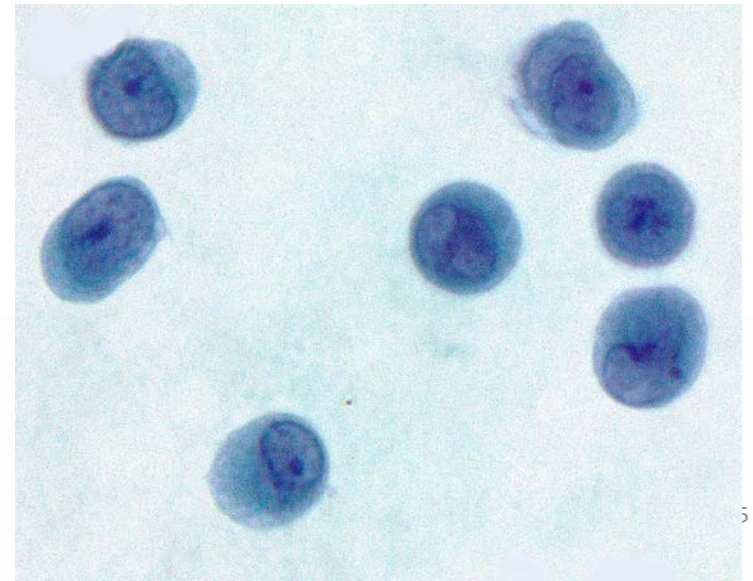
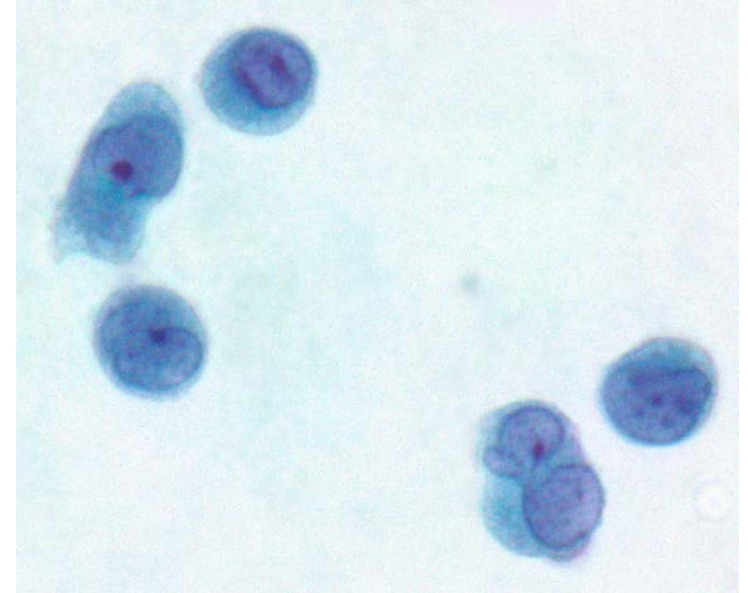
Chronic myeloid leukemia, BCR-ABL1⁺, in blast phase, with PML-RARA⁺

Clinical Course - Continue

- Day 40 BMBx: Relapsed APL (90% cellular; 20% blast)
- Arsenic, ATRA in addition to dasatinib were started
 - Course complicated by possible differentiation syndrome, for which the patient received 3 day course of dexamethasone
- Day 99 BMBx: Remission from APL, but continued chronic phase CML

After the 3rd cycle of arsenic

- The patient presented with severe bilateral frontal headaches associated with nausea, vomiting, photophobia, and dizziness
- CSF fluid: Positive for APL by cytomorphology, flow cytometry, and qRT-PCR



Clinical Course – Continue

- The patient was hospitalized for a total of 102 days in 9 months
- CNS disease did not respond to IT chemotherapy or PETHEMA consolidation (idarubicin, ATRA, and cytarabine)
- The patient died after 7 months of CNS involvement

Discussion

- Our patient never achieved remission from CML
- ABL1 kinase mutation was negative
- Duration from chronic phase to promyelocytic crises: 3 years
- The patient died 17 months after APL was first diagnosed

Review of the literature

- Promyelocytic blast crisis of CML with PML-RARA+ was first reported by Berger et al. in 1983
- Only 12 cases have been reported in the literature
- Age range: 22-85 years (mean: 51)
- M>F
- Duration from chronic phase to blastic crisis: 6 months - 3 years
- Chung et al. and Kashimura et al. reported remission with imatinib in combination with ATRA and arsenic trioxide

| Case/year of pub | age/sex | Duration from CML to blast crisis | Immunophenotyping | Extramedullary APL | Outcome |
|------------------|---------|-----------------------------------|---|--------------------|-------------------------------------|
| 1/1983 | 37/M | 8 months | - | Skin | Died of APL relapse after 16 months |
| 2/1984 | 38/M | 24 months | - | Lymph node | Unknown |
| 3/1987 | 85/F | 10 months | | - | Died of DIC in 2 days |
| 4/1987 | 31/M | 26 months | - | - | Died of DIC within 3 months |
| 5/1990 | 50/M | 3 yrs | | | Unknown |
| 6/1995 | 52/F | 3 yrs | - | - | Died of septic shock after 6 weeks |
| 7/1995 | 55/M | 2 yrs | CD13+, HLA-DR partial (23%); neg for other myeloid and lymphoid markers | - | CML chronic phase; loss f/u |
| 8/1997 | 60/M | 3 yrs | CD45+, CD13+, CD33+, CD34+, CD9+, CD14+ HLA-DR- | - | Died of septic shock within 3 weeks |
| 9/2003 | 22/M | Unknown | Unknown | “CNS Leukemia” | CML chronic phase |
| 10/2008 | 32/M | 6 months | CD13+, CD33+, CD117+; CD34-, HLA-DR- | - | Remission |
| 11/2010 | 69/F | 7 months | CD13+, CD33+ CD34-, HLA-DR- | - | Remission |
| 12/2014 | 82/F | 2 yrs | Unknown | - | Unknown ¹⁹ |

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Final Panel Diagnosis

Chronic myeloid leukemia, BCR-ABL1⁺, in blast phase, with PML-RARA⁺