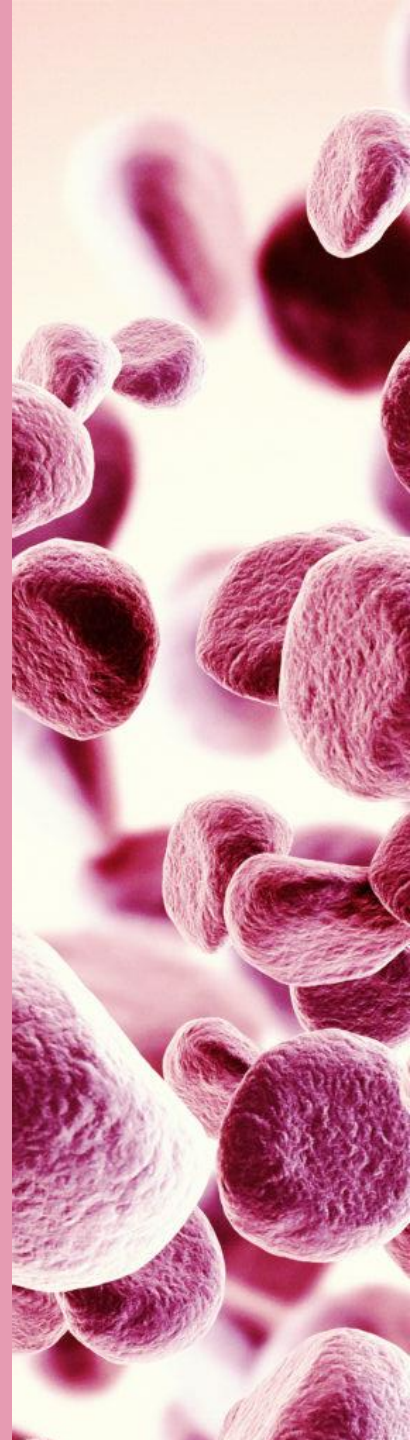
# Äge müeloidleukeemia



| **AML, geneetiliste muutustega** | |
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| AML, t(8;21)(q22;q22); RUNX1-RUNX1T1 | M9896/3 |
| AML, inv(16)(p13.1;q22) või t(16;16)(p13.1;q22); CBFB-MYH1 1 | M9871/3 |
| Äge promüelotsüütleukeemia, t(15;17)(q22;q21); PML-RARA | M9866/3 |
| AML, t(9;11)(p22;q23); MLLT3-MLL | M9897/3 |
| AML, t(6;9)(p23;q34); DEK- NUP214 | M9865/3 |
| AML, inv(3)(q21;q26.2) või t(3;3)( q21;q26.2); RPN1-EVI1 | M9869/3 |
| AML, (megakarüoblastne) t(1;22)(p13;q13); RBM15-MKL1 | M9911/3 |
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| **AML, müelodüsplastiliste muutustega** | M9895/3 |
| **Ravist lähtunud müeloidkasvajad** | M9920/3 |
| **Äge müeloidleukeemia, teisiti täpsustamata** | M9861/3 |
| AML, minimaalse diferentseerumisega | M9872/3 |
| AML, küpsemistunnusteta | M9873/3 |
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| Äge erütroidleukeemia | M9840/3 |
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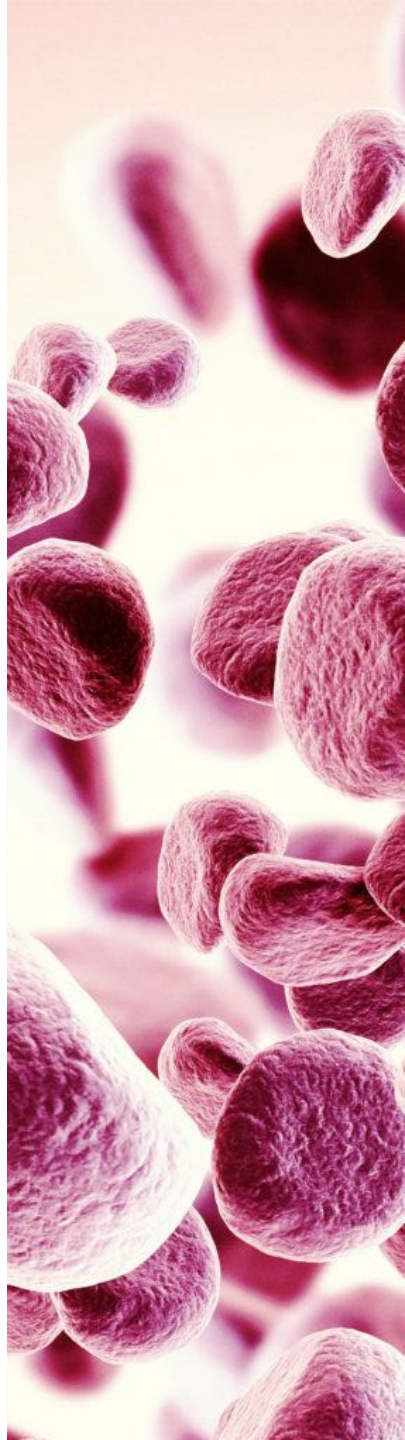
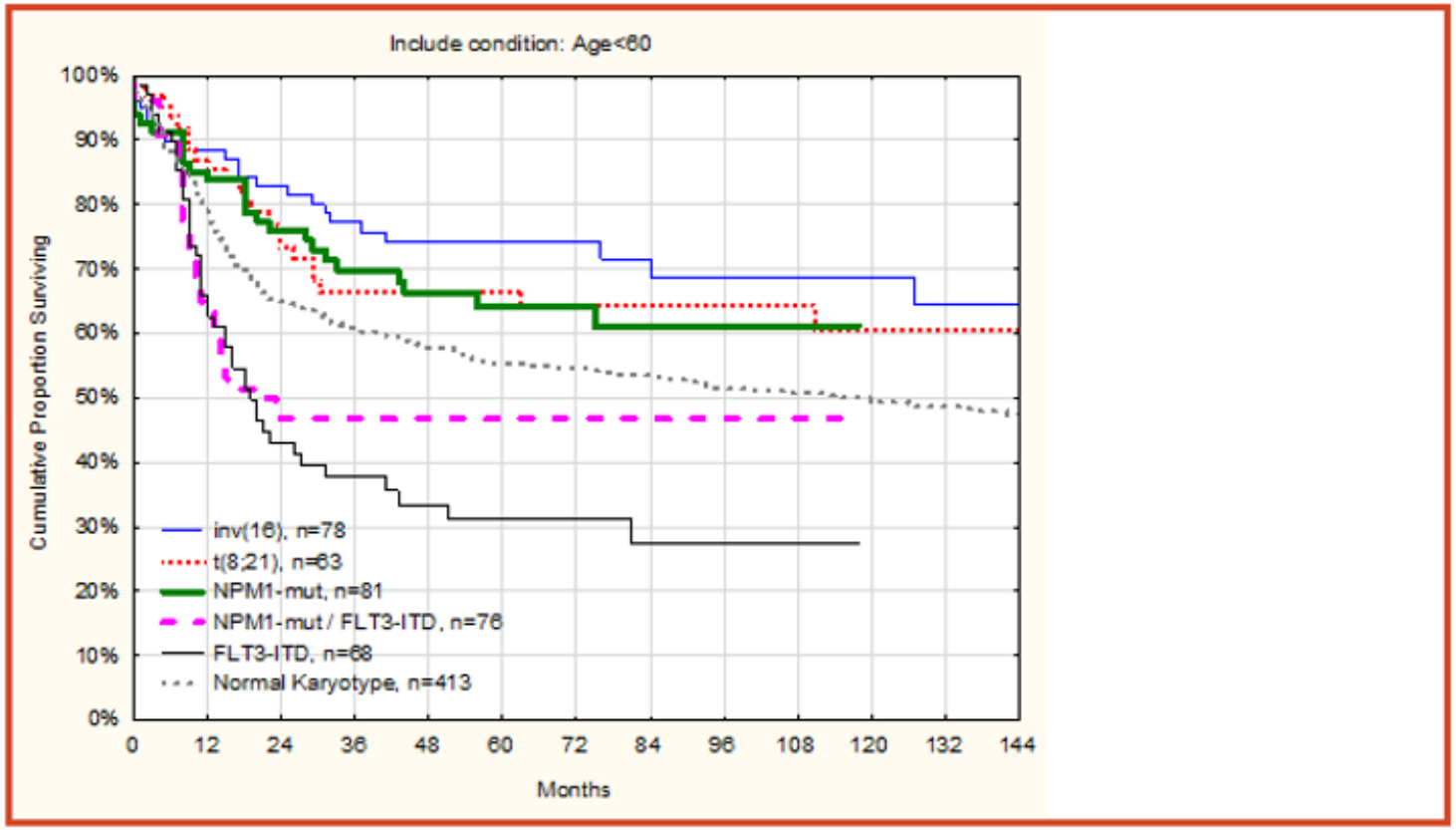
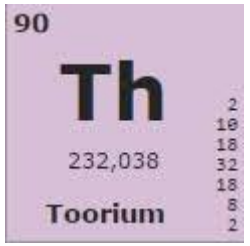
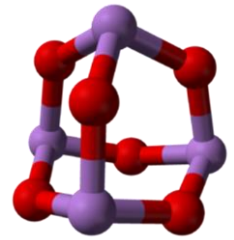
| Äge panmüeloos müelofibroosiga | M9931/3 |
| **Müeloidsarkoom** | M9930/3 |
| **Downi sündroomiga seotud müeloidproliferatsioonid** | |
| Transitoorne müelopoeesi häire | M9898/1 |
| Downi sündroomiga seotud müeloidleukeemia | M9898/3 |
| **Blastne plasmotsütoidne dendriitrakk-kasvaja** | M9727/3 |

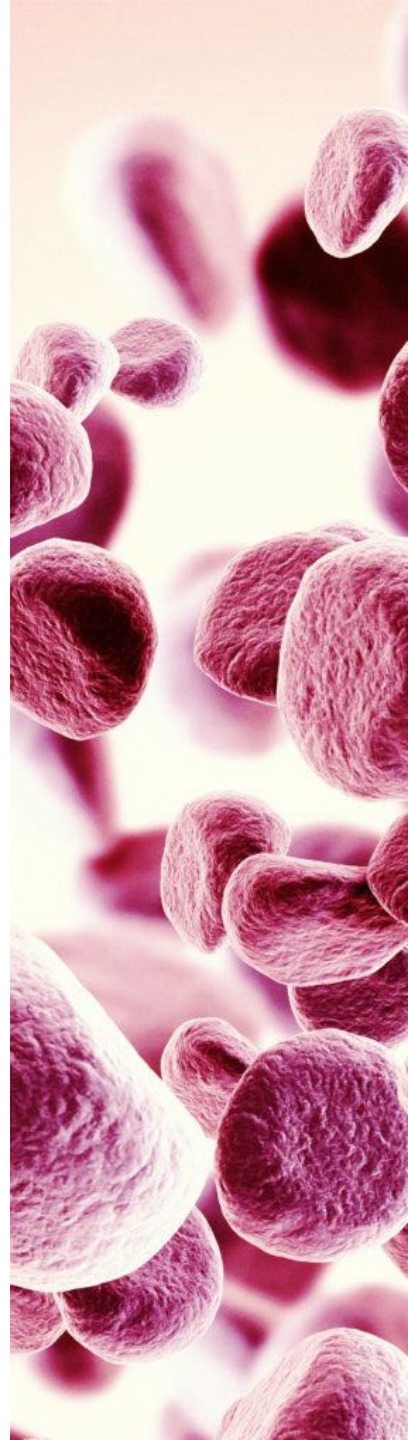



Include condition: Age<60
Cumulative Proportion Surviving
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
12
24
36
48
60
72
84
96
108
120
132
144
Months
inv(16), n=78
t(8;21), n=63
NPM1-mut, n=81
NPM1-mut / FLT3-ITD, n=76
FLT3-ITD, n=68
Normal Karyotype, n=413

- RAT
  - Kiiritus
  - Arseentrioksiid
  - Toorium





# Tsütarabiin

BLOOD *The Journal of Hematology*

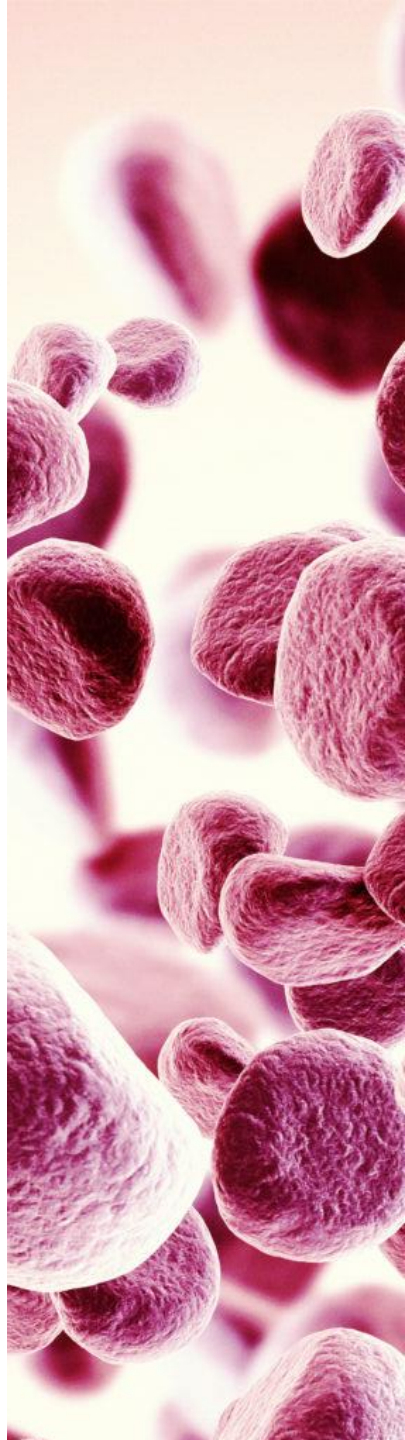
OCTOBER, 1968 VOL. XXXII, NO. 4

## Arabinosyl Cytosine: A Useful Agent in the Treatment of Acute Leukemia in Adults

*By* Rose Ruth Ellison, James F. Holland, Marise Weil, Claude Jacquillat, Michel Boiron, Jean Bernard, Arthur Sawitsky, Fred Rosner, Bernard Gussoff, Richard T. Silver, Arthur Karanas, Janet Cuttner, Charles L. Spurr, Donald M. Hayes, Johannes Blom, Louis A. Leone, Farid Haurani, Robert Kyle, J. L. Hutchison, R. Jackson Forcier and John H. Moon

ARABINOSYL CYTOSINE (ara-C) is a synthetic pyrimidine nucleoside differing in the sugar moiety from the normal metabolites cytidine and deoxycytidine. (Fig. 1). It is cytotoxic to mammalian cells in culture,[1] inhibits a number of DNA viruses,[2,3,4] and shows in vivo antitumor activity against leukemia L1210[5,6] and a variety of transplanted rodent neoplasms.[7,8]

Talley and Vaitkevicius[9] reported a series of 13 patients treated with ara-C. These investigators administered the drug intravenously rapidly with doses



# Daunorubitsiin

BLOOD *The Journal of Hematology*

VOL. XLI, NO. 4 APRIL 1973

## Acute Promyelocytic Leukemia: Results of Treatment by Daunorubicin

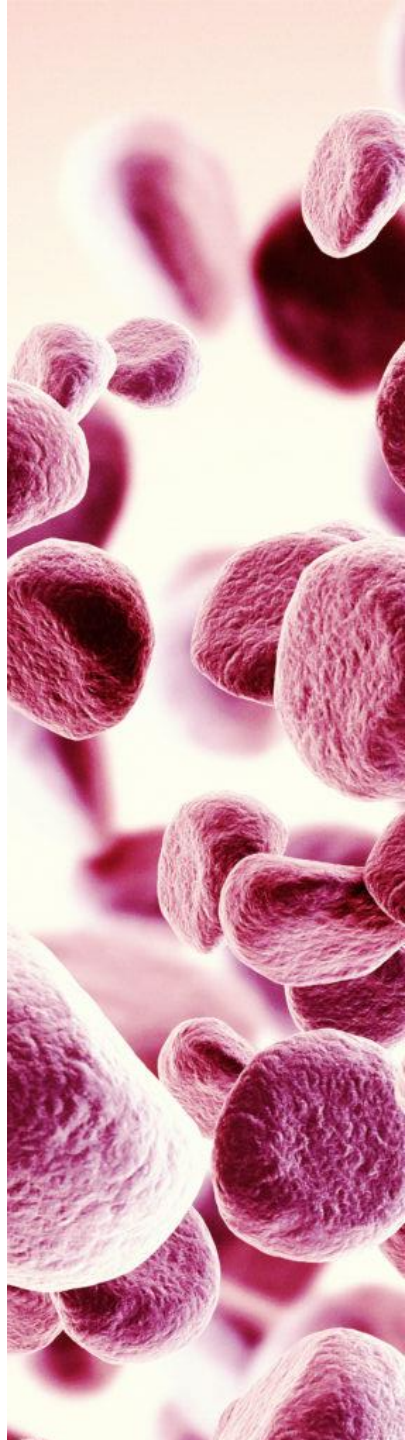
By Jean Bernard, Marise Weil, Michel Boiron, Claude Jacquillat, Georges Flandrin, and Marie-François Gemon

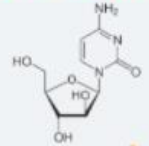
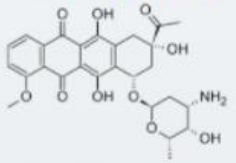
Daunorubicin induces complete remissions in about 50% of patients with acute promyelocytic leukemia. The median duration of these remission is 26 mo. Failures are mainly due to hemorrhages as a result of disseminated intravascular coagulation during the first 5 days (25%) or due to sepsis during the second and third week (25%). Long-term survivals are more frequent than in the other acute granulocytic leukemias.

FOLLOWING THE FIRST REPORT of acute promyelocytic leukemia,[1] we gave a complete description of this variety of acute leukemia in 20 patients.[2] The distinct cellular morphology, severity of hemorrhages secondary to fibrinopenia, as well as its fulminant course, were characteristic and led to a separate classification of acute promyelocytic leukemia (APL). Since 1967, we have used daunorubicin in the treatment of 44 patients with APL and in this report we compare the results of such treatment with the course of 36 patients treated up to 1967 before the drug was available. The striking sensitivity of APL to daunorubicin has completely changed its prognosis and will undoubtedly lead to renewed interest in this unique form of acute leukemia.

### MATERIALS AND METHODS

This report includes 80 patients with APL; 73 in our department and 7 patients of Professor B. Dreyfus; all were seen between 1963 and 1971. The limited number of patients confirms the relative rarity of this disease; approximately 5% of all acute leukemias. The age and sex distribution are shown in Table 1. As was pointed out



| Drug | Doses | Days | Delivery |
|---|---|---|---|
| Cytosine arabinoside (NSC-638678)  | 100 mg/m² | 1 2 3 4 5 6 7 | Continuous infusion |
| Daunorubicin (NSC-83142)  | 45 mg/m² | 1 2 3 4 5 6 7 | Intravenous |

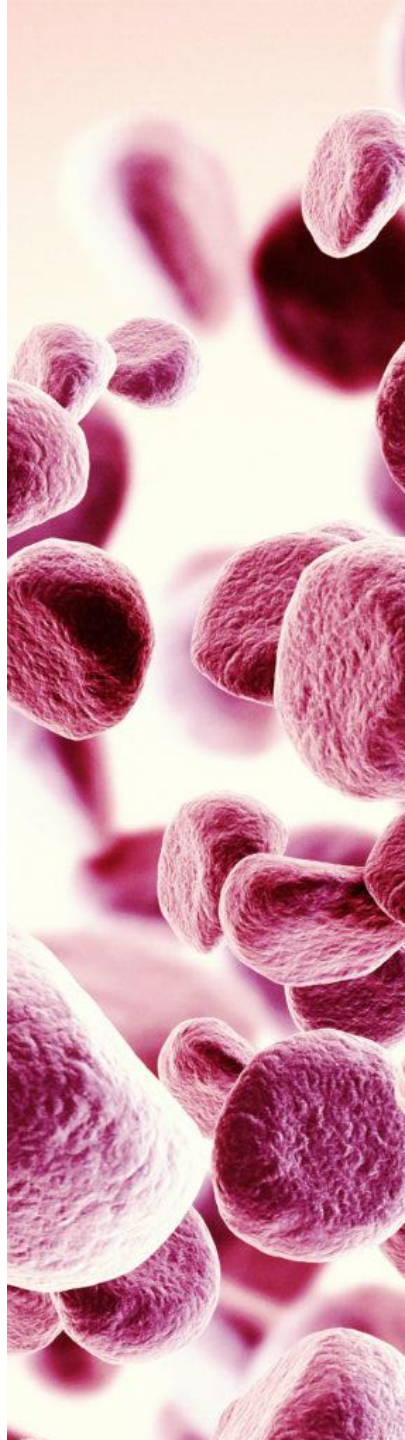
## The "7+3" Regimen

1973

**16** patients with AML, age 17-78 years

5/8 previously untreaded — CR

2/8 previously treaded — CR



# Management of Adult Acute Myelogenous Leukaemia

D. CROWTHER, R. L. POWLES, C. J. T. BATEMAN, M. E. J. BEARD, C. L. GAUCI, P. F. M. WRIGLEY, J. S. MALPAS, G. HAMILTON FAIRLEY, SIR RONALD BODLEY SCOTT

*British Medical Journal*, 1973, **1**, 131–137


## Summary

**Consecutive adult patients admitted to St. Bartholomew's Hospital with acute myelogenous leukaemia have been treated with a remission induction drug schedule consisting of daunorubicin and cytosine arabinoside. Intermittent five-day courses were used in 72 patients, and a complete remission was obtained in 39 patients (54%). An alternative drug schedule in 22 patients resulted in fewer remissions but this may have been due to age differences in the two groups. Age and initial platelet count were found to be important factors in determining the success of remission induction therapy; the older patients and those with low platelet counts responded less well.**

**A series of 23 patients who achieved remissions was divided into two groups; one received intermittent combination chemotherapy as the only form of maintenance, and the other was given weekly immunotherapy in addition to the chemotherapy. The immunotherapy consisted of irradiated allogeneic leukaemic cells and B.C.G. Eight of the 10 patients on chemotherapy alone have already relapsed compared with five out of 13 patients in the immunotherapy group. It is hoped that these promising initial results with this form of maintenance will be confirmed as more patients enter the maintenance trials.**

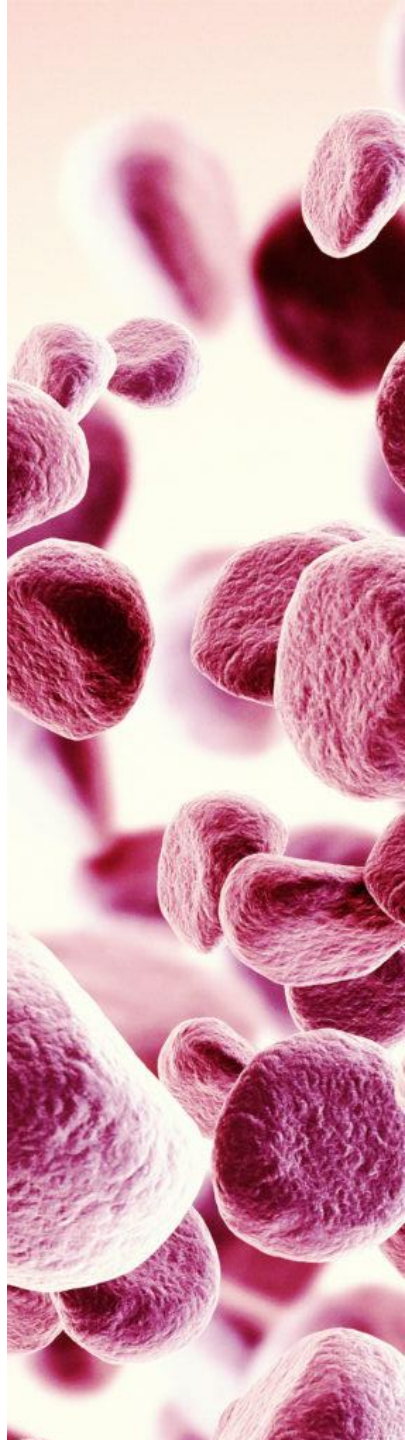

## Introduction

Much has been written in recent years about the treatment of acute lymphoblastic leukaemia, in which the aim is now to eradicate the disease with the hope of permanent cure. The situation in acute myelogenous leukaemia is different. Until recently, it was rare to obtain complete remissions in this disease and difficult to maintain them for any length of time. There are now several regimens in existence which produce complete remissions in about half of the patients. We have used a combination of daunorubicin and cytosine arabinoside which, when used as single agents, give a higher percentage of remissions than any other single agent, and our preliminary results in 37 patients were reported by Crowther *et al.* (1970).

The purpose of this paper is to record our experience at St. Bartholomew's Hospital of treating 94 patients since 1969 with these two drugs, because they highlight many of the difficulties. Firstly, the difficulty of obtaining a remission and the complications which arise during this time; secondly, the problems arising during the maintenance of remission; thirdly, the problem of those who do not remit; and, finally, the treatment of the relapsed patients.

## Materials and Methods

*Patients.*—Altogether, 94 unselected patients with acute myelogenous leukaemia have been admitted to three trials since May



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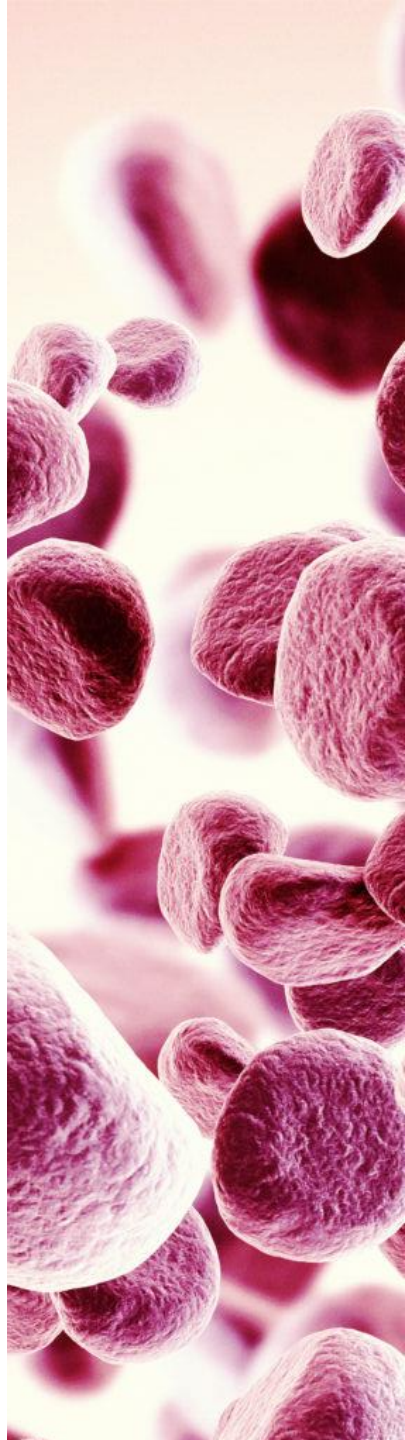
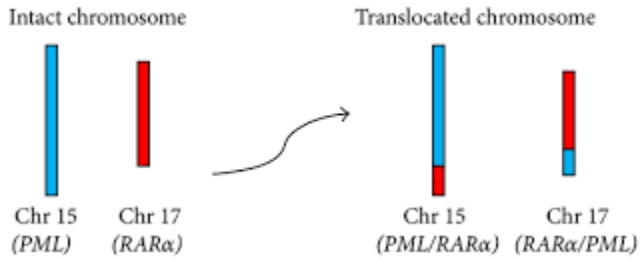
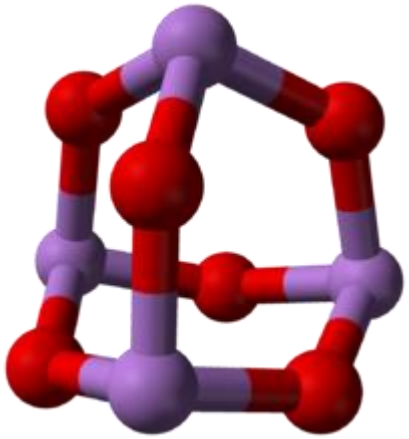


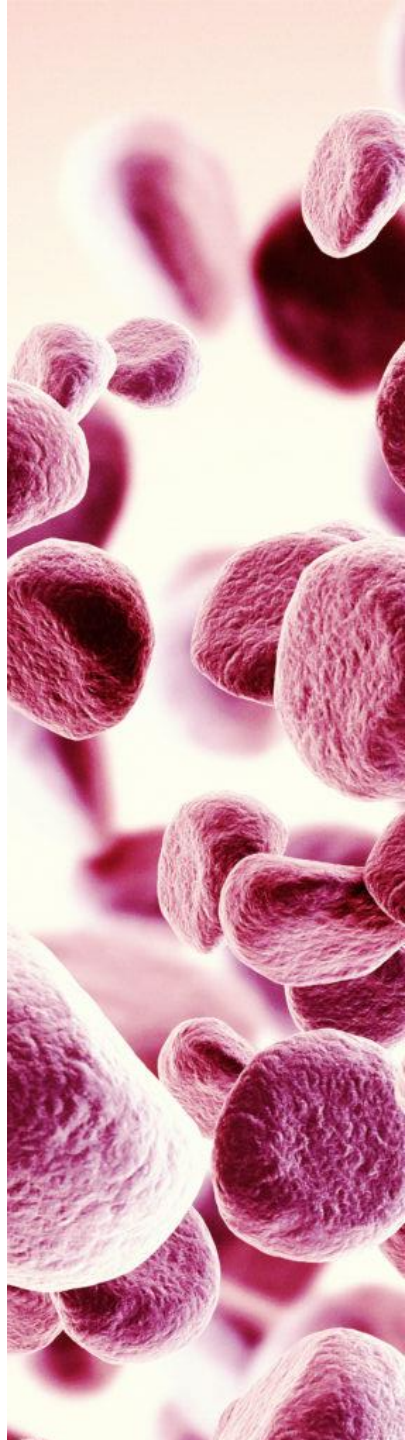

Intact chromosome
Translocated chromosome
Chr 15
(PML)
Chr 17
(RARα)
Chr 15
(PML/RARα)
Chr 17
(RARα/PML)

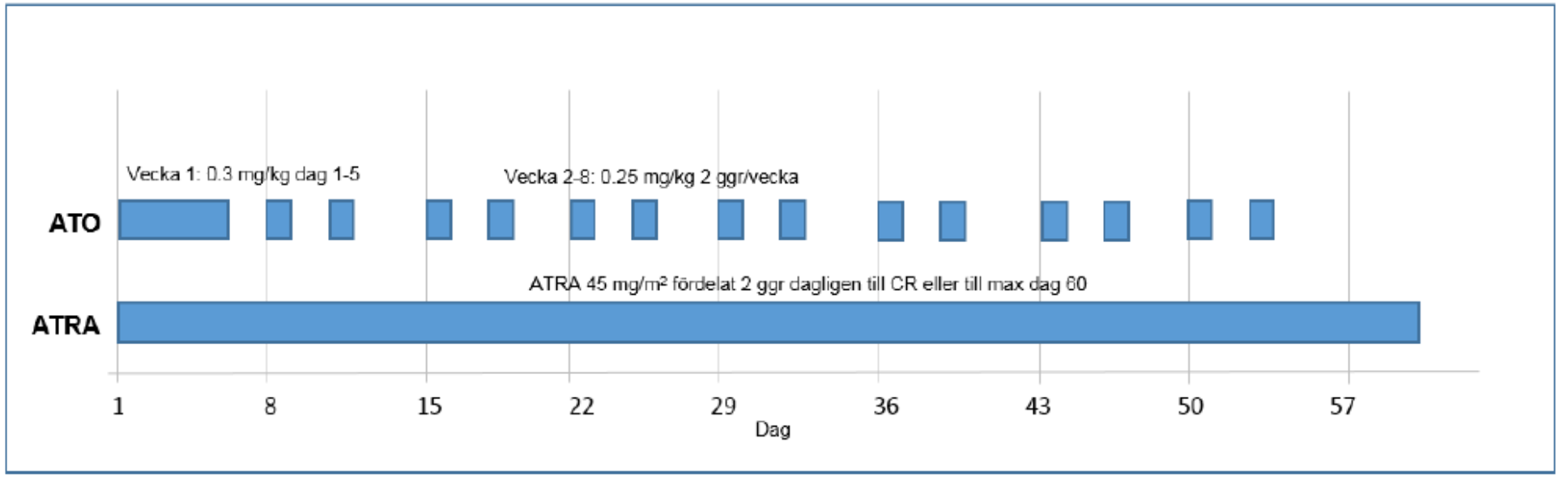
# Diarseentrioksiid

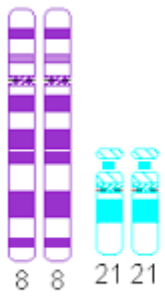


**Päranduspulber**

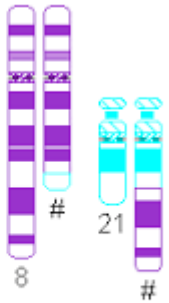
- Paljudes Euroopa riikides müüsid illegaalsed diilerid arseeni sisaldavat “päranduspulbrit” (*poudre de succession, inheritance powder*).
- Napoleon
- Tšaikovski




Vecka 1: 0.3 mg/kg dag 1-5
Vecka 2-8: 0.25 mg/kg 2 ggr/vecka
ATO
ATRA 45 mg/m² fördelat 2 ggr dagligen till CR eller till max dag 60
ATRA
1
8
15
22
29
36
43
50
57
Dag



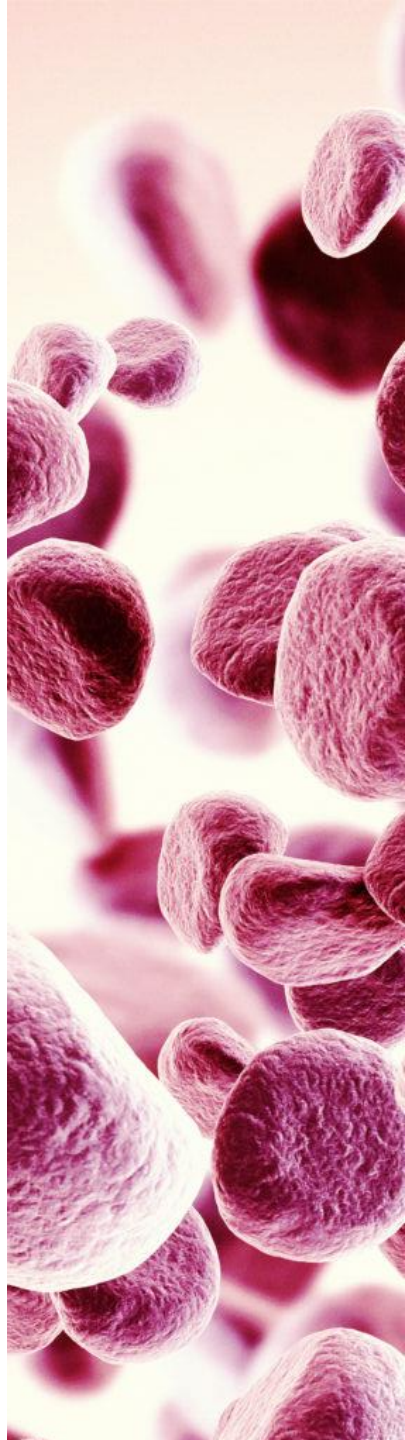

Normal




t(8;21)(q22;q22)


Normal


inv(16)(p13q22)



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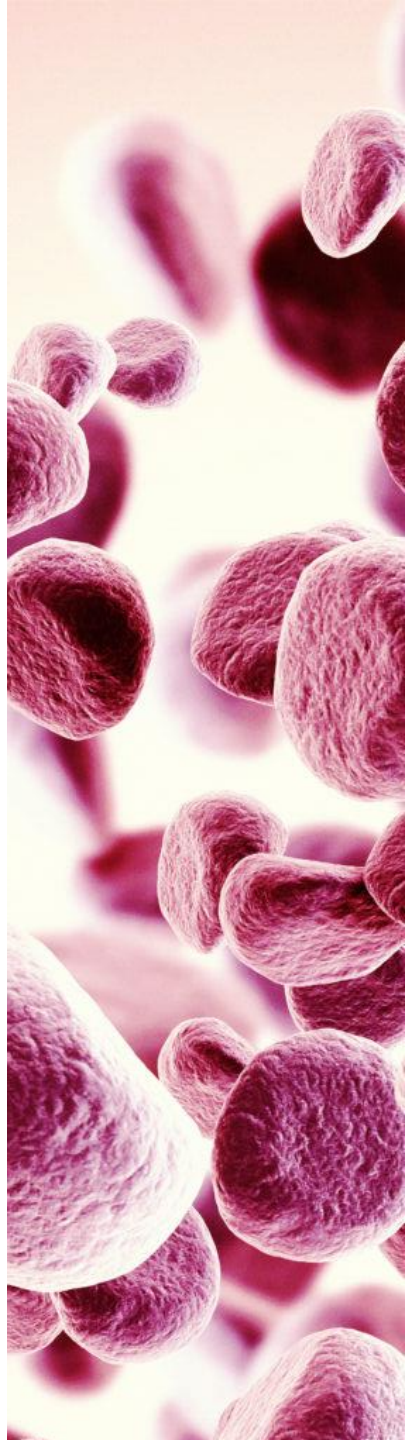
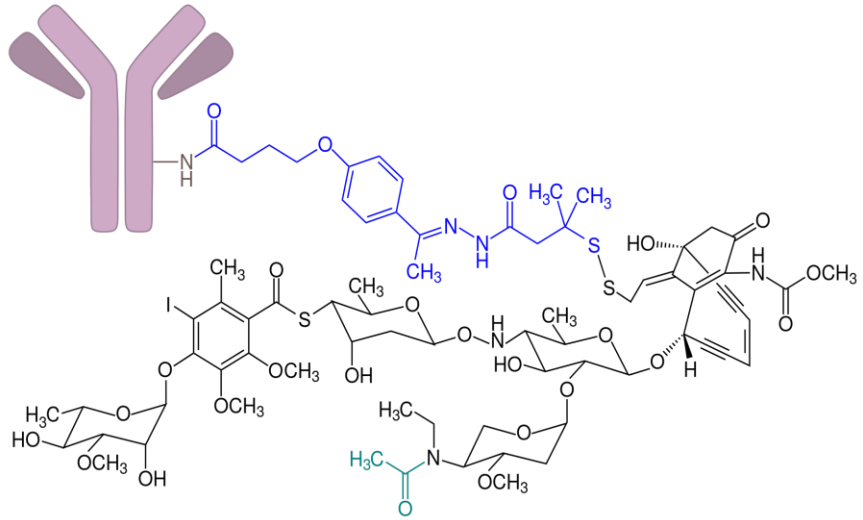
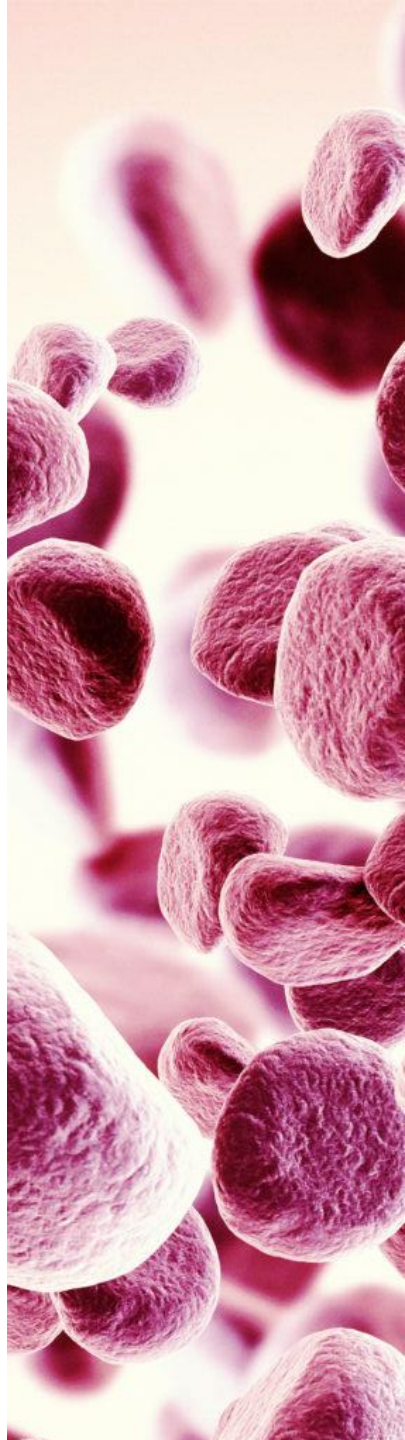
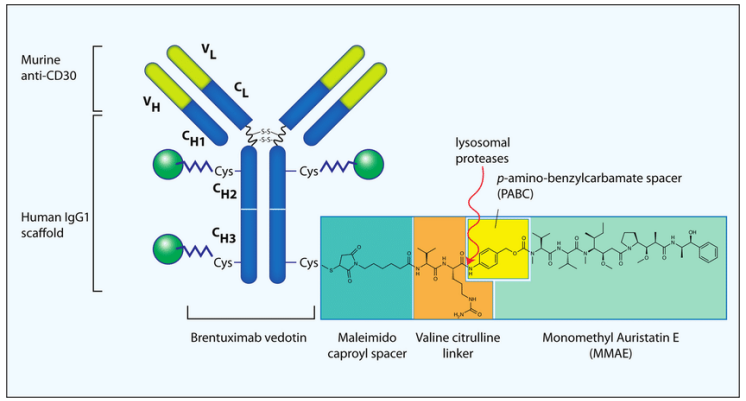


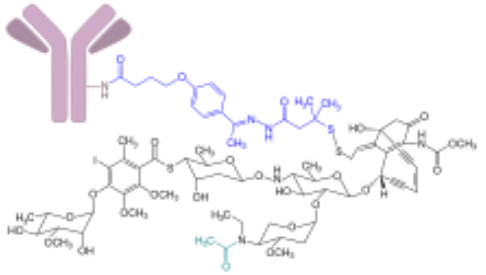
# Gemtuzumab ozogamicin- Mylotarg

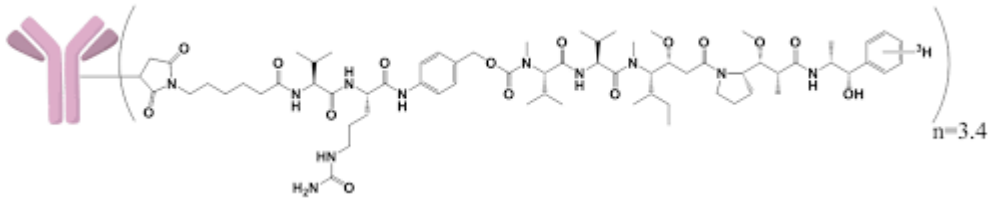


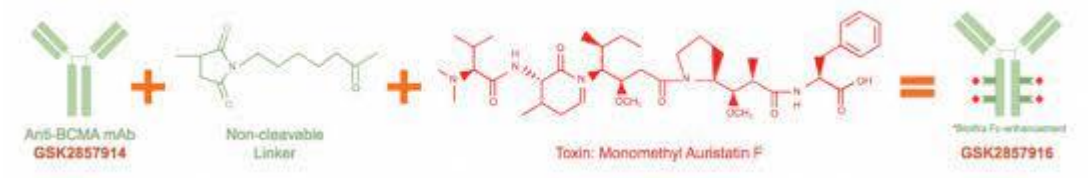



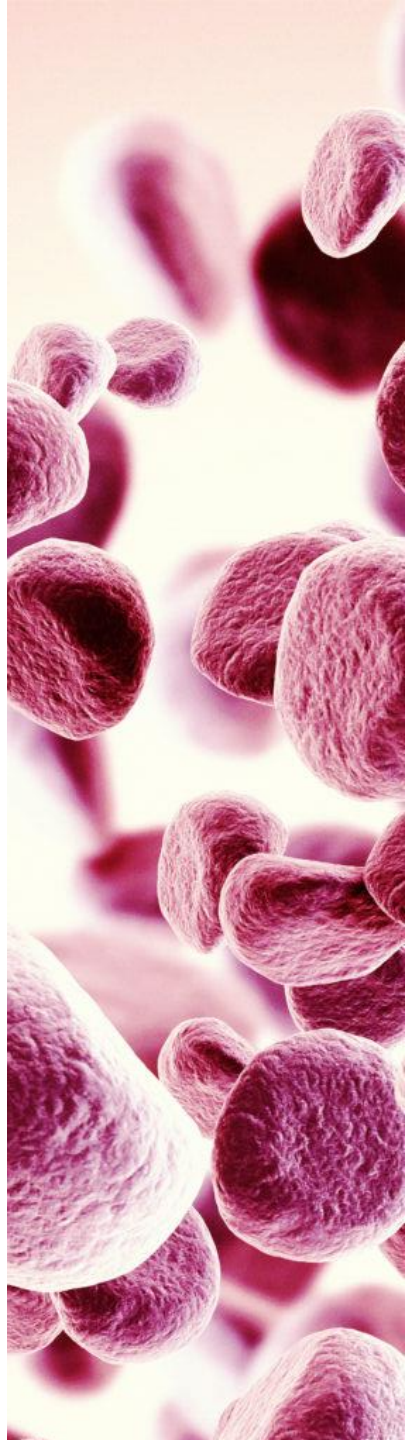
# Brentuksimab- Adcetris  Inotuzumab- Besponsa
# Polatuzumab- Polivy  Belantamab- Blenrep



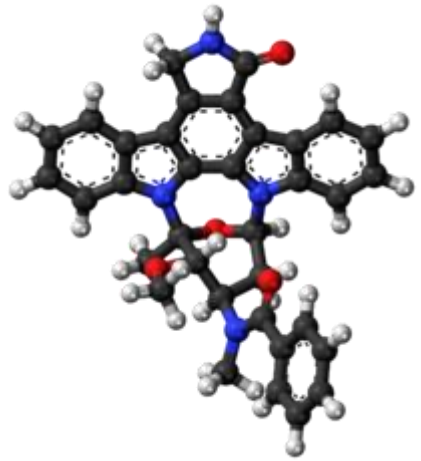



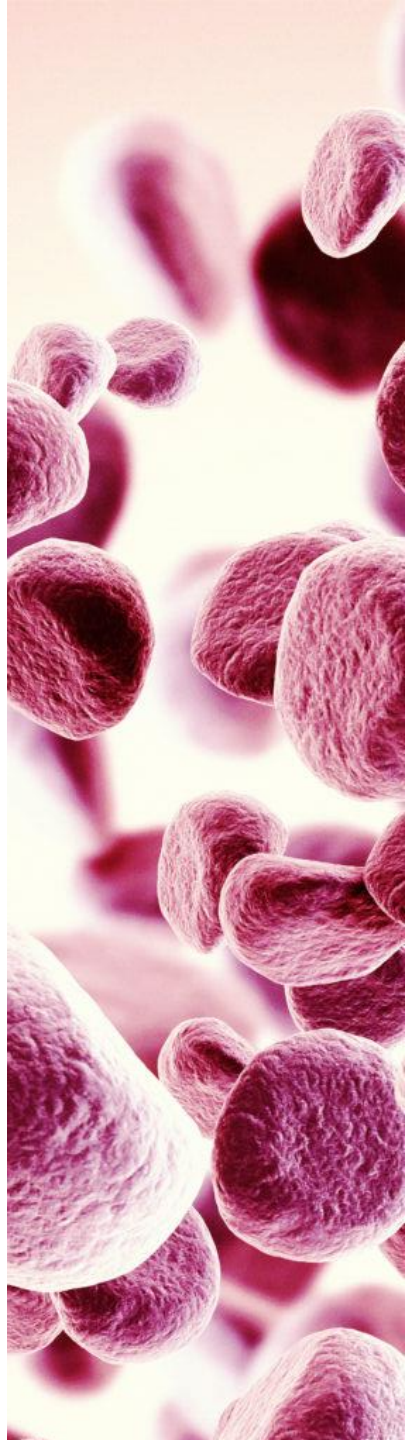


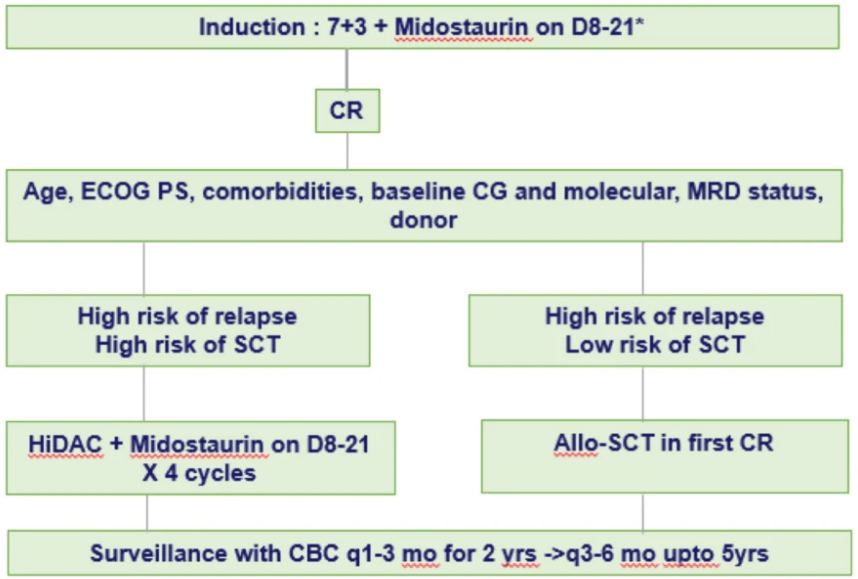
# Midostauriin- Rydapt





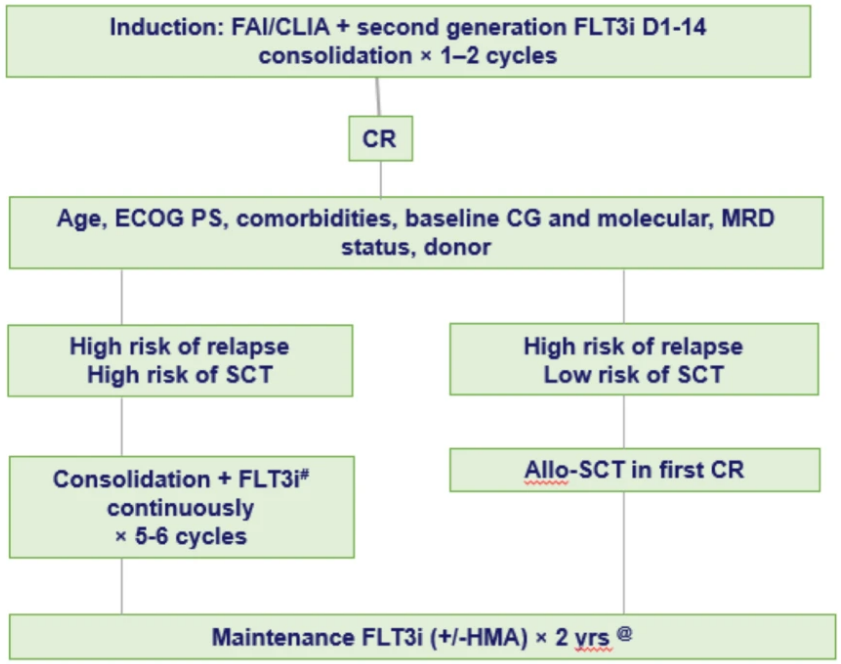
**A**

★Conventional Approach in *FLT3* mutated AML patients Eligible for Intensive Chemotherapy




**B**

★The MD Anderson approach in *FLT3* mutated AML patients eligible for Intensive Chemotherapy



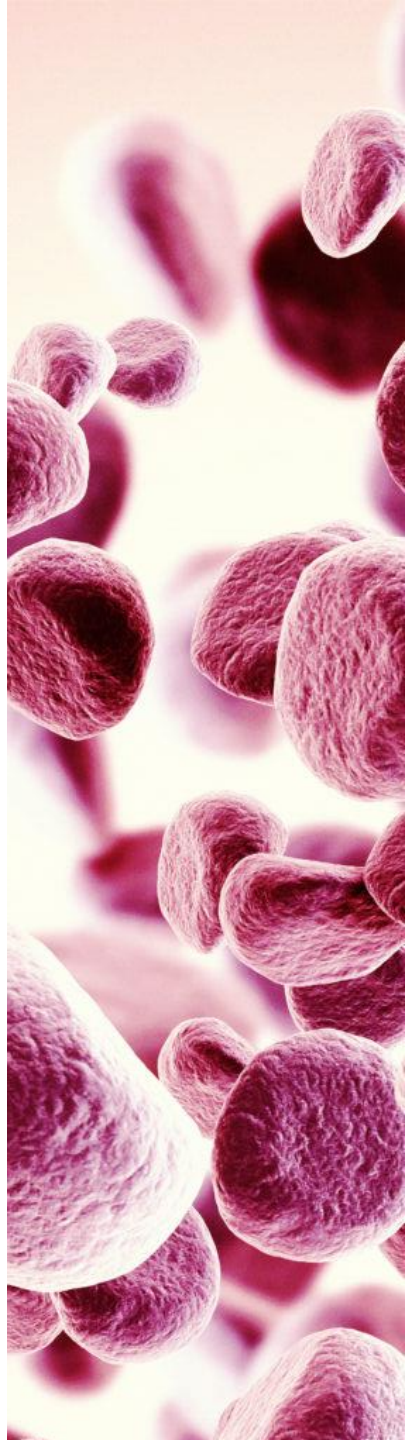

★ Assess patients for clinical trial options

* - Bone marrow assessment on D21

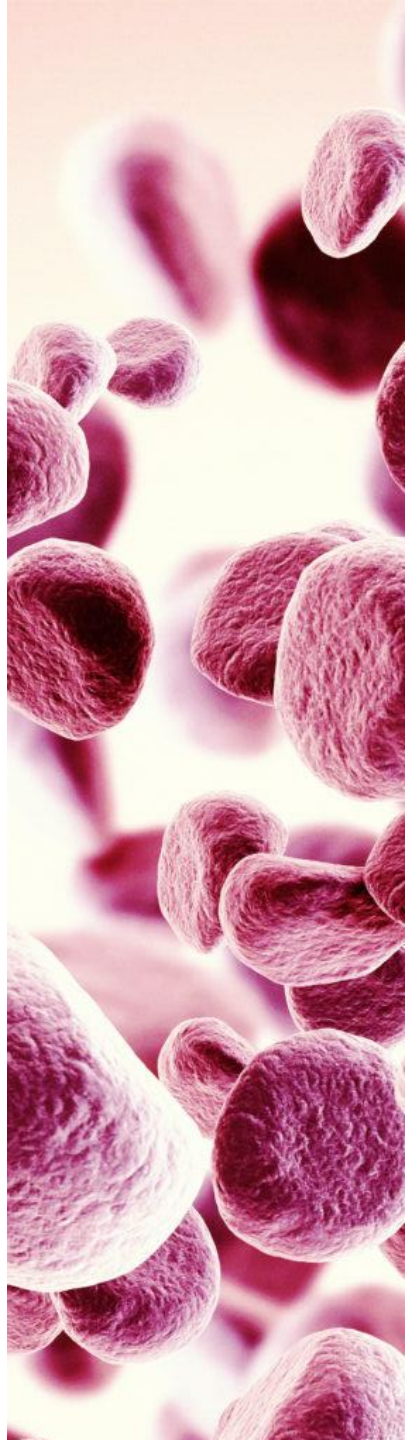
#We prefer second generation FLT3 inhibitor for our patients in all settings.

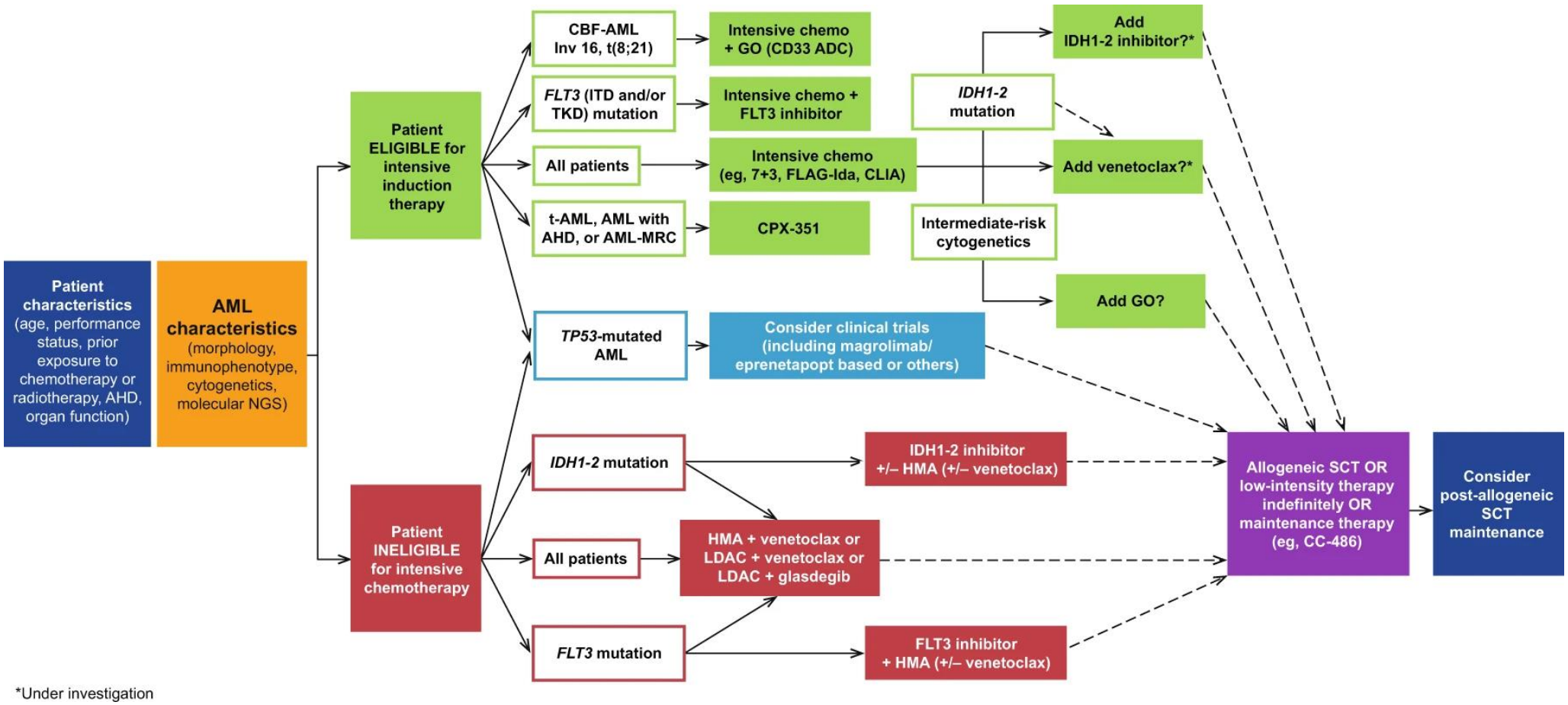
We advocate maintenance therapy with HMA and FLT3i combination in young and fit patients not eligible for Allogenic Stem Cell Transplant (ASCT)

@Ideal duration of FLT3i maintenance is not defined but we recommend at least 2 years maintenance, and in most cases prefer indefinite maintenance if good tolerability



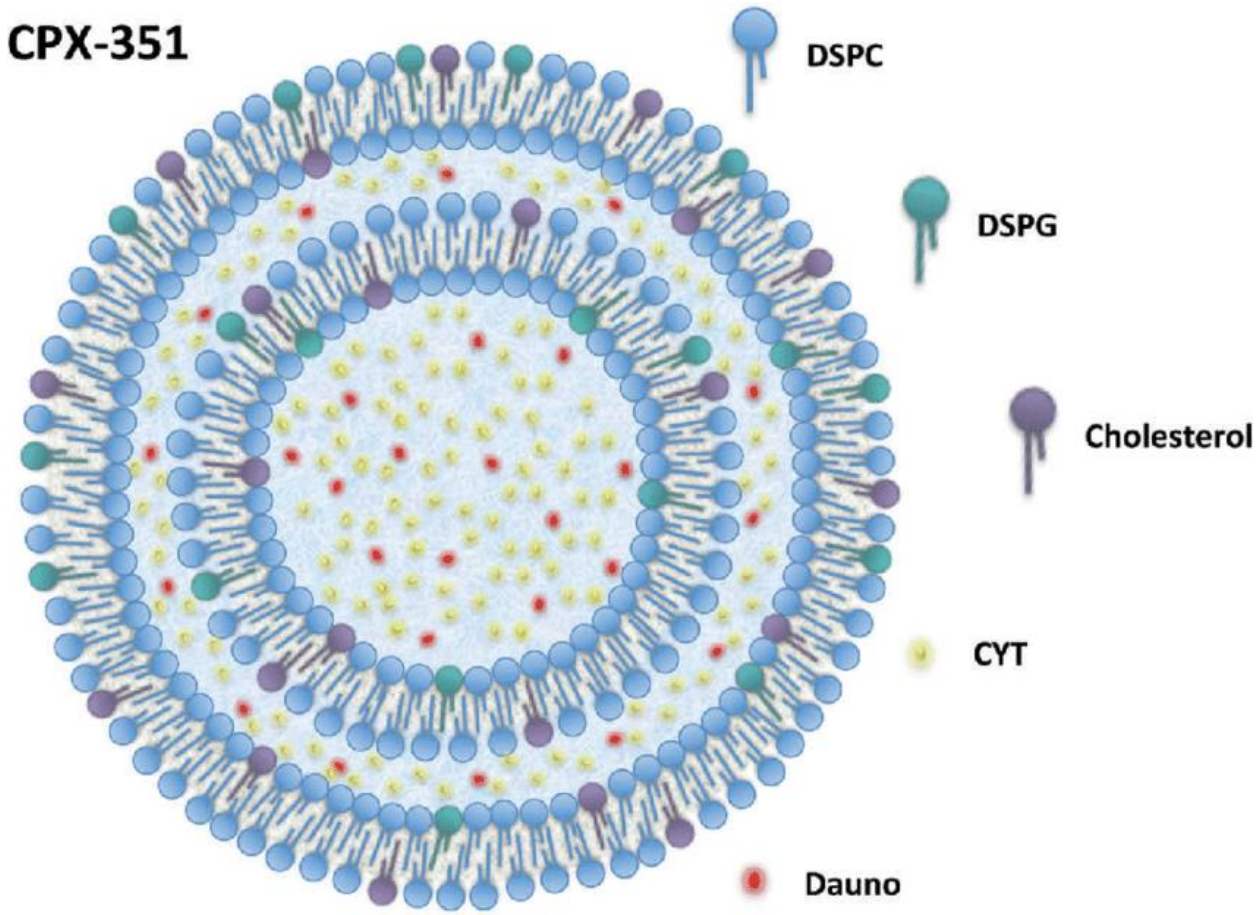
| | |
|---|---|
| 1960s | Use of chemotherapy for AML introduce |
| 1970s | Cytarabine plus anthracycline regimens (eg, 7 + 3) standard of care |
| 1980 | In younger AML patients, ASCT demonstrates OS advantage |
| 2000 | FDA approves gemtuzumab ozogamicin for R/R AML; subsequently withdrawn (2010) due to toxicities |
| 2012 | EMA (not FDA) approves decitabine for older patients with AML |
| 2015 | EMA (not FDA) approves azacitidine for older patients with AML >30% blasts |
| 2017–2018 | FDA approves |
| | CPX-351 for untreated t-AML or AML-MRC |
| | Gemtuzumab ozogamicin ± induction for CD33+ AML |
| | Enasidenib for R/R *IDH2*-mut AML |
| | Midostaurin plus induction/consolidation chemo for newly diagnosed *FLT3*-mutant AML |
| | Ivosidenib for R/R *IDH1*-mutant AML |
| | VEN + LDAC/HMA for untreated AML (older or unfit) |
| | Glasdegib plus LDAC for untreated AML (older or unfit) |
| | Gilteritinib for R/R *FLT3*-mutant AML |

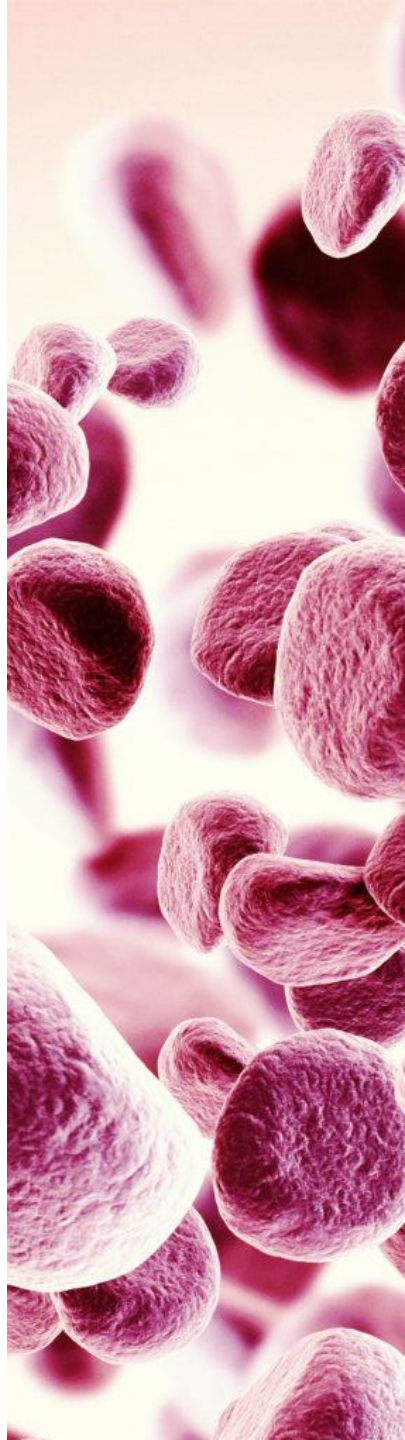




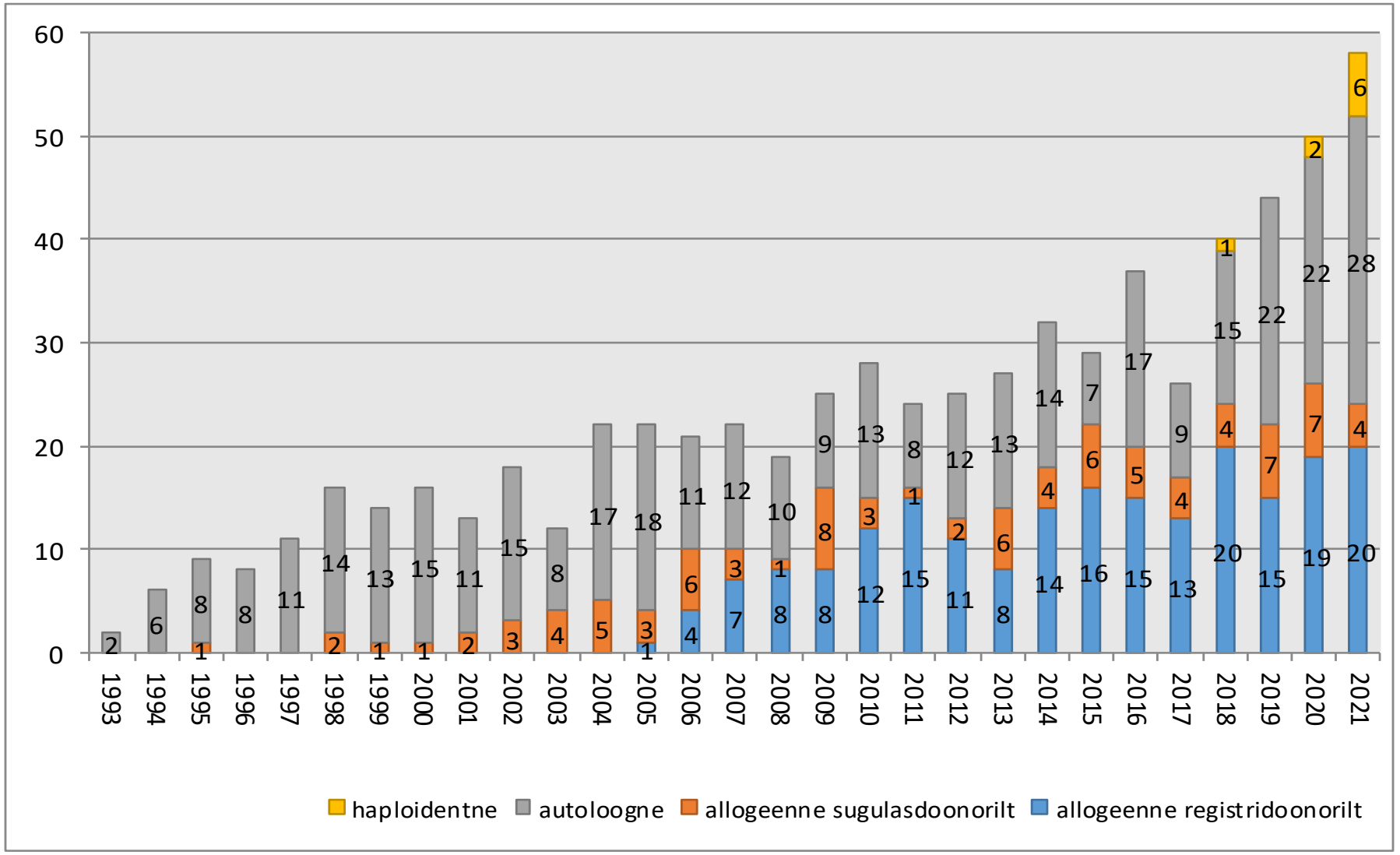

Daver et al. Blood Cancer Journal (2020) 10:107
https://doi.org/10.1038/s41408-020-00376-1

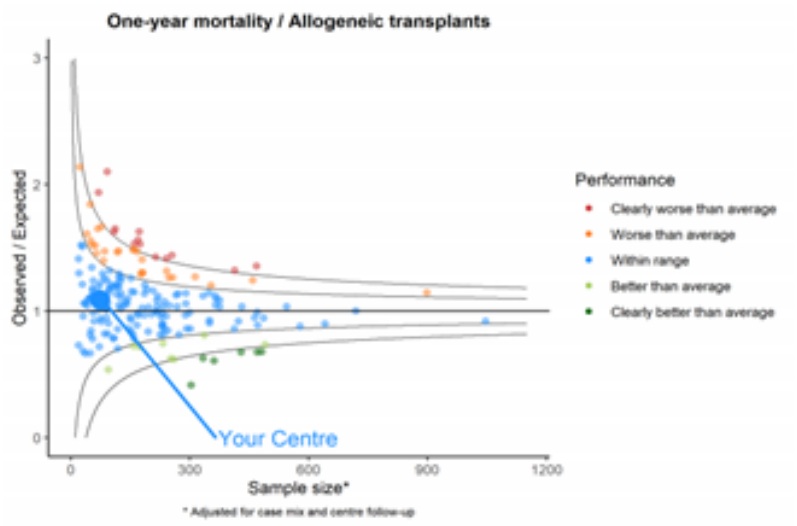
# CPX-351- Vyxeos



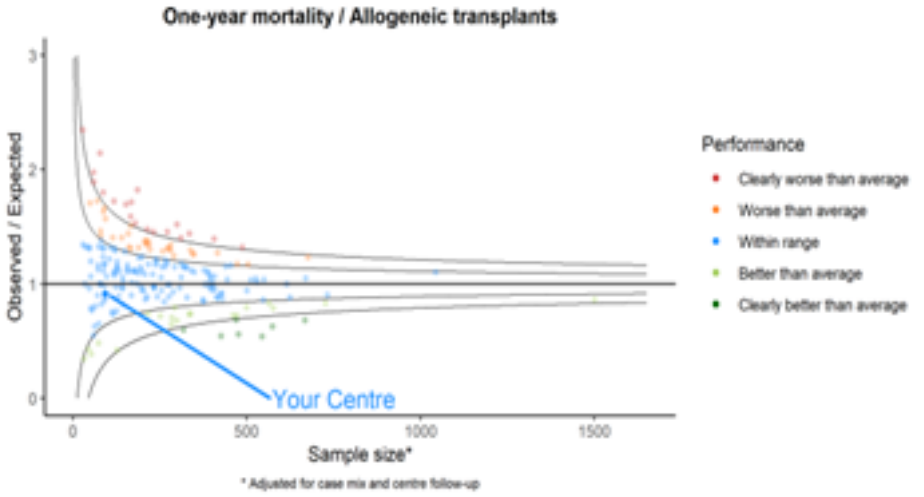
# Siirdamiste arv






Funnel plot of 1-year mortality following allogeneic transplantation comparing observed over expected mortality adjusted for case mix and centre follow-up. Results are highly affected by quality of follow-up over the period.

Lehterdiagramm Tartu Ülikooli Kliinikumi allogeense siirdamise patsientide 1- aasta suremus perioodil 2013- 2016 võrrelduna teiste EBMT keskustega

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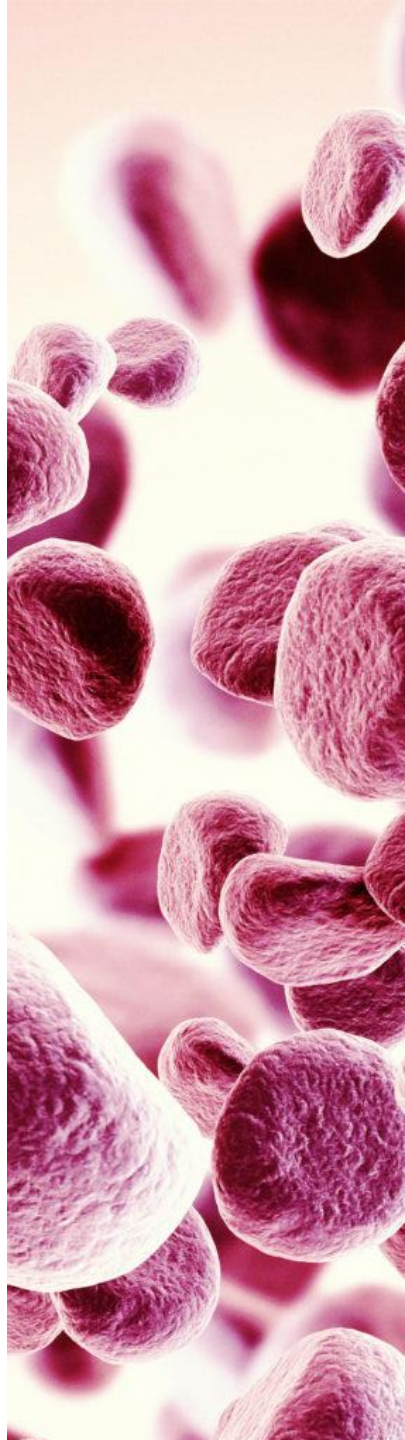
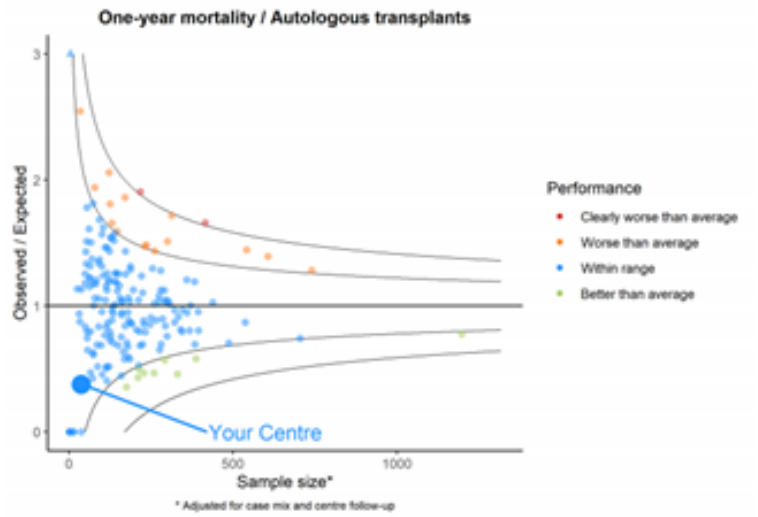
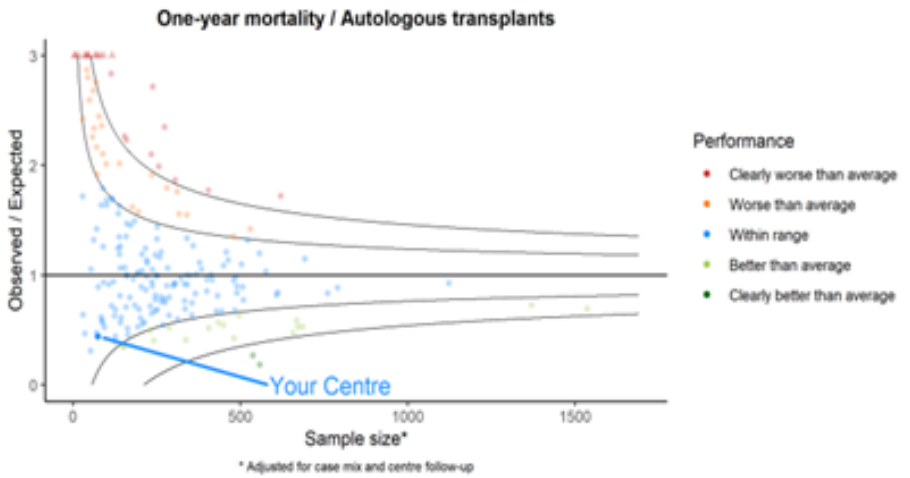




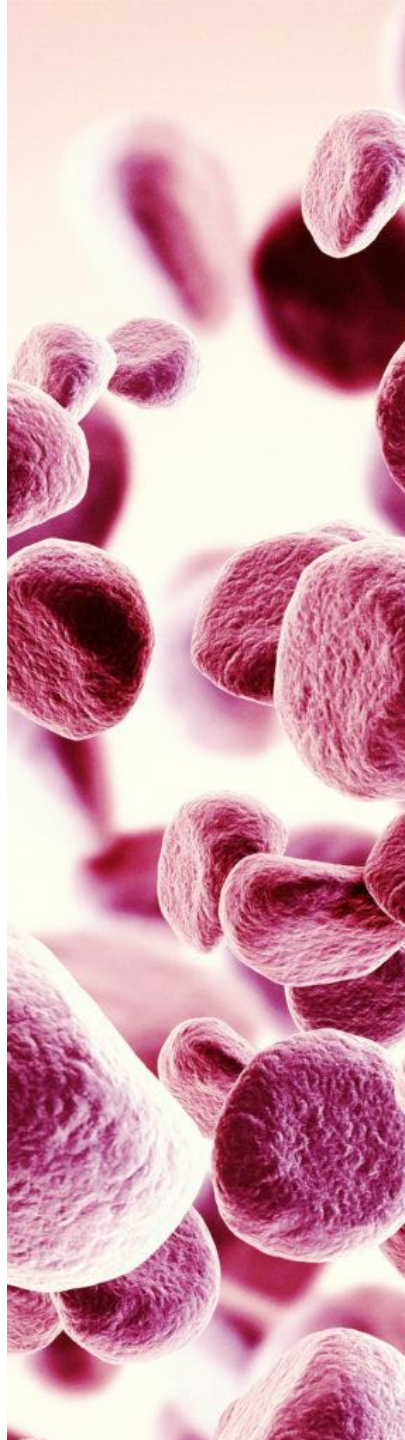

Funnel plot of 1-year mortality following autologous transplantation comparing observed over expected mortality adjusted for case mix and centre follow-up. Results are highly affected by quality of follow-up over the period.

Lehterdiagramm Tartu Ülikooli Kliinikumi autoloogse siirdamise patsientide 1- aasta suremus perioodil 2013- 2016 võrrelduna teiste EBMT keskustega




Funnel plot for 1-year mortality following autologous transplantation comparing observed over expected mortality adjusted for case mix and centre follow-up. Results are highly affected by quality of follow-up over the period.

Lehterdiagramm Tartu Ülikooli Kliinikumi autoloogse siirdamise patsientide 1- aasta suremus perioodil 2015- 2019 võrrelduna teiste EBMT keskustega



# Clinimacs Prodigy