CANCER RESEARCH UK - AML19 TRIAL:

Improving treatment for Acute Myeloid Leukaemia (AML) and High-Risk Myelodysplastic Syndrome (MDS)

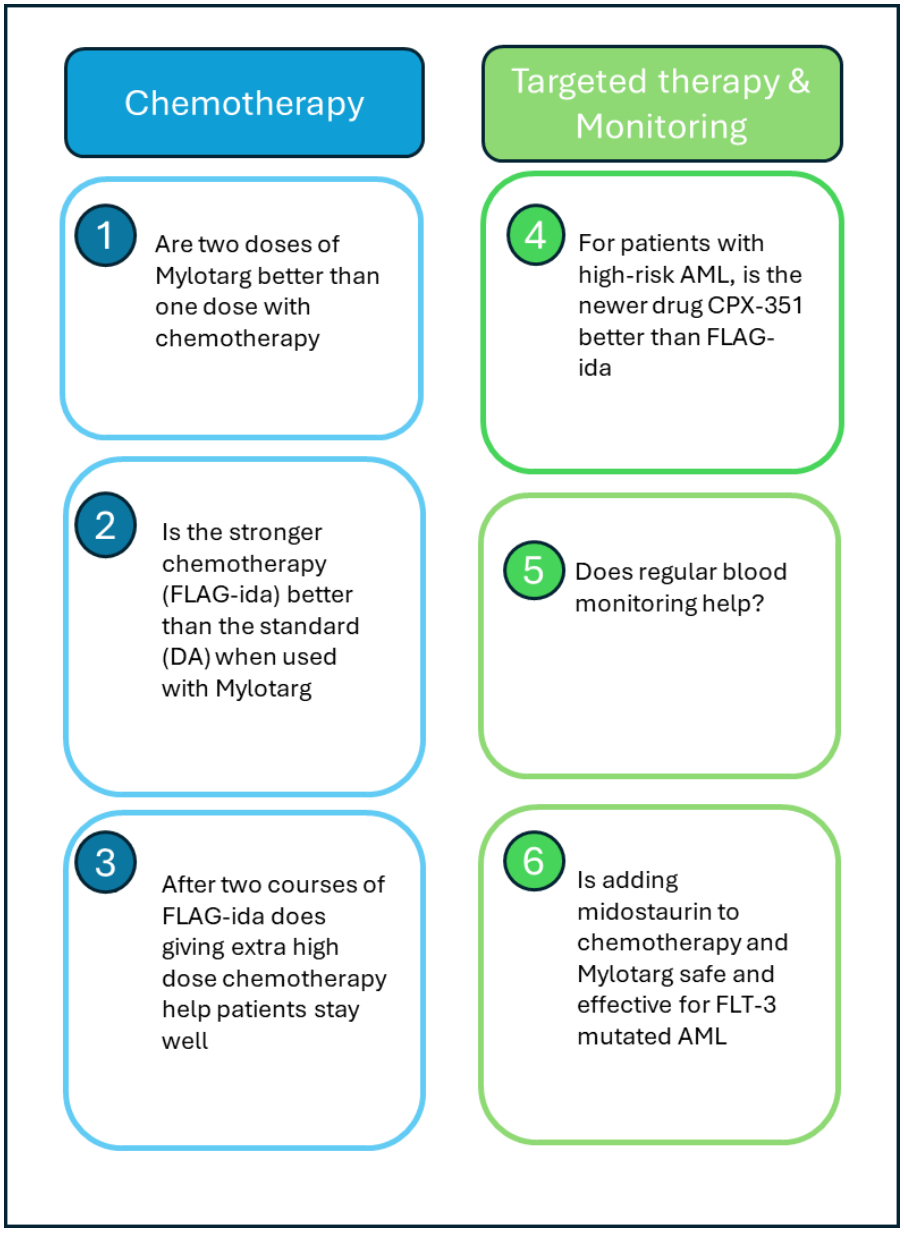
TRIAL SUMMARY FOR PATIENTS AND FAMILIES

Thank you to all the patients and families who took part in this important research.

Between 2014-2021, over 2,000 patients across 104 hospitals in the UK, Denmark, and New Zealand helped us learn more about how to treat AML and MDS better.

What was the AML19 trial about?

The trial asked 6 key questions to improve treatment for patients with AML or high-risk MDS



TRIAL OUTCOMES – WHAT WE FOUND

1️⃣ Are two doses of Mylotarg better than one dose with chemotherapy?

- **Answer:** No. The results showed no overall survival benefit for two Mylotarg doses vs a single dose. This means that one dose remains the standard treatment and may also help reduce the risk of side effects.

2️⃣ Is the stronger FLAG-Ida chemotherapy better compared to standard DA chemotherapy?

- **Answer:** Yes. The combination of the treatment regime FLAG-Ida chemotherapy with Mylotarg significantly reduced the risk of AML coming back (relapse).

3️⃣ Does extra high-dose chemotherapy after FLAG-Ida help patients stay well for longer?

- **Answer:** Not clearly. Adding extra chemotherapy did not clearly improve results. Results varied based on the genetic changes or type of leukaemia. This is explained in more detail below.

🧬 Genetic Findings:

- Some patients with certain genetic changes in their leukaemia cells (called NPM1 or FLT3) did especially well with FLAG-Ida + Mylotarg.
- Patients with a different type of AML, known as core binding factor AML, actually did best with the standard DA + Mylotarg treatment.

HOW CAN THIS HELP FUTURE PATIENTS:

- ✓ For patients with newly diagnosed AML who are not in the highest risk group, the combination of **FLAG-Ida + Mylotarg** lowered the chance of the leukaemia coming back. This means fewer patients needed extra chemotherapy later or a stem cell transplant.

- ✓ For patients whose leukaemia cells have certain **genetic changes** (called *NPM1* or *FLT3*), **FLAG-Ida + Mylotarg** worked especially well and gave much better long-term results.

- ✓ For those with **core binding factor AML**, the **standard DA + Mylotarg** remains the best choice.

- ✓ Doctors can now better **match the treatment to each patient's type of AML**, giving the most benefit while avoiding unnecessary side effects.

Learn more in the full paper: JCO Article

TRIAL OUTCOMES – WHAT WE FOUND

4 Is CPX-351 better than FLAG-Ida for high-risk AML?

189 participants took part. They were randomly given either CPX-351 or FLAG-Ida as their first treatment.

- **Answer:** CPX-351 didn't help everyone more than FLAG-Ida.

- But it did help some patients with specific genetic changes, especially those linked to myelodysplastic syndromes (MDS).
- CPX-351 did not help patients stay well longer overall compared to FLAG-Ida.
- CPX-351 did, however, lower the chance of relapse (the leukaemia coming back).
- Patients who were able to have a stem cell transplant while their leukaemia was in remission tended to do the best in the long term.

HOW CAN THIS HELP FUTURE PATIENTS:

- ✓ CPX-351 may not be better for all high-risk patients, but it could help some people with specific genetic changes in their leukaemia.
- ✓ This shows how important fast genetic testing is at diagnosis, so doctors can decide if CPX-351 is the right choice for each patient.

Learn more in the full paper: **Blood Advances**

TRIAL OUTCOMES – WHAT WE FOUND

5 Does regular blood monitoring help?

637 participants were randomly assigned to either standard of care or regular monitoring (extra blood and bone marrow tests to check for very small amounts of leukaemia left after treatment)

- **Answer:** Not for everyone.
- For most patients, regular monitoring did not make a difference compared with standard care.
- But for patients whose leukaemia had certain genetic changes (NPM1 and FLT3), monitoring helped patients live longer and stay well.

HOW CAN THIS HELP FUTURE PATIENTS:

✓ For patients with NPM1 or FLT3 mutations, molecular monitoring has now become part of standard care, helping doctors make better treatment decisions at the right time.

Learn more in the full paper in *The Lancet Haematology*: Read here

TRIAL OUTCOMES – WHAT WE FOUND

6 Does adding midostaurin help patients with FLT3-mutated AML?

77 participants with FLT3-mutated AML took part in this part of the AML19 trial. All participants received chemotherapy and Mylotarg, and were also given midostaurin, a targeted drug taken during and after treatment.

- **Answer:** It was safe and effective.
- Most patients responded well, and over 75% were doing well two years later.
- The treatment was generally well tolerated, with very few serious side effects early on.
- Follow-up tests showed that most patients had no signs of leukaemia after treatment, meaning the added drug (midostaurin) may have helped clear the disease more effectively.

HOW CAN THIS HELP FUTURE PATIENTS:

✓ Adding midostaurin to this combination of chemotherapy and Mylotarg appears to be both safe and effective for patients with FLT3-mutated AML.

✓ Because of these promising results, this treatment is now being studied further in a larger trial called OPTIMISE-FLT3. If the results are confirmed, this approach could lead to better outcomes and become a new standard treatment for future patients with this type of leukaemia.

Learn more in the full paper in Blood Advances: Read here

Thank You

Professor Russell and the AML19 team extend their heartfelt thanks to all the patients and families for their invaluable participation and support.

We are also deeply grateful to the sponsors, laboratories, hospitals, and dedicated staff across the UK, Denmark, and New Zealand who made this trial possible.

If you have any questions please do not hesitate to contact the study team AML19@cardiff.ac.uk