**98-A (n = 633) NON-Randomised**

**Risk-Adapted Therapy of Acute Myeloid Leukemia of Adults (18-60 Years) According to the Cytogenetic Result**

Risk adapted for younger adults by risk group where:

High risk : refractory disease after first induction therapy **and/ or** abn 3q, -5/-5q, -7/-7q, abn 12p, abn 17p, and complex

Intermediate: achieved CR after induction **and/ or** intermediate risk karyotype (normal, 11q23, 16q22, other)

Low-risk: complete remission after induction therapy **and** low risk karyotype [t(8;21)]

**Treatment**:

ICE/ICE (– for responders to 1st ICE)/HAM consolidation (for CR patients) /

* if intermediate risk and HLA match then allo TPL
* if intermediate +NK and no related donor 🡪 randomization autologous TPL or HAM
* if intermediate and no
* high risk patients a allogeneic transplantation is assigned from a related or unrelated donor preferentially after a dose-intensified conditioning therapy.
* Other intermediate 🡪 autologous
* second consolidation stratified by risk definition
* if low risk 🡪 second course of HAM

ICE/A-HAM – for refractory to ICE

**Papers:**

Schlenk et al. Prospective evaluation of allogeneic hematopoietic stem-cell transplantation from matched related and matched unrelated donors in younger adults with high-risk acute myeloid leukemia: German-Austrian trial

AMLHD98A. J Clin Oncol. 2010 Oct 20;28(30):4642-8. Epub 2010 Aug 30.

Schlenk RF, Döhner K, et al Mutations and treatment outcome in cytogenetically normal acute myeloid leukemia. N Engl J Med. 2008 May 1;358(18):1909-18.

**98-B True randomised(n = 177)**

* **61 years, de novo or secondary AML**

Patients were randomized via a telephone call :

Induction/ consolidation OR induction /consolidation +ATRA

IF CR or partial remission (PR) 🡪 ICE /A-ICE

IF (RD) 🡪 A-HAE.

Allogeneic transplantation was allowed for patients with an HLA-identical family donor on the decision of the local investigator.

Second randomization was performed after completion of first consolidation therapy for patients in CR. Patients were randomized to either a second intensive consolidation therapy OR maintenance

In data summarized as St therapy n = 77, St therapy +ATRA n = 81, AIDA n =9, Pilotphase n =10

**Papers:**

Schlenk et al. Phase III study of all-trans retinoic acid in previously untreated patients 61 years or older with acute myeloid leukemia. Leukemia. 2004 Nov;18(11):1798-803.

Fröhling et al. Cytogenetics and age are major determinants of outcome in intensively treated acute myeloid leukemia patients older than 60 years: results from AMLSG trial AML HD98-B.Blood. 2006 Nov 15;108(10):3280-8. Epub 2006 Jul 13.

Schlenk, Döhner K, et al. Gene mutations and response to treatment with all-trans retinoic acid in elderly patients with acute myeloid leukemia. Results from the AMLSG Trial AML HD98B.Haematologica. 2009 Jan;94(1):54-60. Epub 2008 Dec 4.

**07-04**

This trial is a study on all-trans retinoic acid in combination with induction and consolidation therapy as well as pegfilgrastim after consolidation therapy in younger patients with newly diagnosed acute myeloid leukemia (AML).

This is also a risk adapted “randomization” trial but as the trial as such is not published I am not sure what the exact criteria are. !!!However in Gaidzik paper it says that similar to the 98A paper that :

* patients with a matched related donor were allocated to allogeneic stem cell transplantation
* patients who failed to achieve a complete remission (CR), and all patients (with FLT3-ITD–positive AML) who entered the trial after April 2006 were scheduled to receive allogeneic stem cell (SC) transplant from either MRD or matched unrelated donor (MUD).

The final randomization arms are as follows:

1. standard therapy (n = 290)
2. Standard therapy intergroup (n = 47) …ps Lars thought these two are best kept separate but not sure whether they should as in their papers they discuss 4 arms.
3. St Therapy ATRA + VPA (n = 54)
4. ATRA(n = 295)
5. VPA (n = 63)

**Papers**

Gaidzik VI, Bullinger L, Schlenk RF, Zimmermann AS, Röck J, Paschka P, Corbacioglu A, Krauter J, Schlegelberger B, Ganser A, Späth D, Kündgen A, Schmidt-Wolf IG, Götze K, Nachbaur D, Pfreundschuh M, Horst HA, Döhner H, Döhner K. RUNX1 mutations in acute myeloid leukemia: results from a comprehensive genetic and clinical analysis from the AML study group. J Clin Oncol. 2011 Apr 1;29(10):1364-72. Epub 2011 Feb 22.

Kayser S, Schlenk RF, Londono MC, Breitenbuecher F, Wittke K, Du J, Groner S, Späth D, Krauter J, Ganser A, Döhner H, Fischer T, Döhner K; German-Austrian AML Study Group (AMLSG). Insertion of FLT3 internal tandem duplication in the tyrosine kinase domain-1 is associated with resistance to chemotherapy and inferior outcome. Blood. 2009 Sep 17;114(12):2386-92. Epub 2009 Jul 14.

Schlenk RF, Döhner K, Kneba M, Götze K, Hartmann F, Del Valle F, Kirchen H, Koller E, Fischer JT, Bullinger L, Habdank M, Späth D, Groner S, Krebs B, Kayser S, Corbacioglu A, Anhalt A, Benner A, Fröhling S, Döhner H; German-Austrian AML Study Group (AMLSG). Gene mutations and response to treatment with all-trans retinoic acid in elderly patients with acute myeloid leukemia. Results from the AMLSG Trial AML HD98B. Haematologica. 2009 Jan;94(1):54-60. Epub 2008 Dec 4.