Research - Study Office News:

- analysis of data collected in the EBMT Registry on a cohort of patients receiving plerixafor
- plerixafor off-label transplant use study
- iron toxicity after allo-SCT in untreated MDS/CMML;
- evaluation of the effect of prior therapy with Nilotinib or Dasatinib on the outcome after allogeneic stem cell transplantation for adult patients with Chronic Myeloid Leukemia

Analysis of data collected in the European Group for Blood and Marrow Transplantation (EBMT) Registry on a cohort of patients receiving plerixafor(Non-Interventional Prospective Study CALM)

In the European Union, the label for plerixafor is indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood (PB) for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma whose cells mobilise poorly. The EMA license for plerixafor requires Genzyme to undertake monitoring of the outcome of patients transplanted with plerixafor mobilised cells and compare these to equivalent patients transplanted without the use of plerixafor in order to rule out a potential role for plerixafor in mobilizing malignant cells and thus contributing to disease relapse after the autologous stem cell transplantation (ASCT). For this purpose Genzyme and EBMT have developed the CALM study: a collaboration to Collect Autologous transplant outcomes in Lymphoma and Myeloma patients (CALM). Eligible for the study are adult patients with data reported to the EBMT, who have lymphoma or multiple myeloma and received their first ASCT of PB non ex-vivo manipulated stem cells between 1 January 2008 and 31 December 2011, using cells mobilised with plerixafor plus G-CSF (or plus chemotherapy) or mobilised with G-CSF alone (or plus chemotherapy). Annual Follow Up reports are collected for at least a further 3 years during 2012, 2013 and 2014 (i.e., individual patients will have 3 to 7 years of follow up depending on the date of transplantation).

The CALM study started in April 2011. Approximately 50 centers from 19 countries have registered for participation, expecting to collect over 7500 transplantations, of which estimated 47% multiple myeloma and 53% lymphoma transplantations. The figure below shows that more than 650 transplantations are expected to be treated with plerixafor mobilised stem cells. The center registration phase of this study is coming to an end and the focus of the study is now shifting to the data collection phase. The data request combines a complete MED-B and 4-page MED-C questionnaire for every transplantation. The data flow has started up well. So far, 173 completed MED-B and 347 MED-C forms have been received. The participating centers, not performing their own data entry, are asked to send the MED-B data for their prospective transplantations (not yet registered in ProMISe) to the EBMT Data Office in London where they will be entered. The MED-B data for the retrospective transplantations (already registered in ProMISe) as well as the MED-C data for all transplantations are entered by the EBMT Data Office in Leiden and have to be sent there.

Figure 1: Expected number of transplantations
For more information about the CALM study, please have a look at the EBMT website or contact study coordinator Marcha Suits at the EBMT Data Office in Leiden via e-mail address: calmembt@lumc.nl.

Q&A sessions next EBMT Annual Meeting in Geneva!

At the 38th Annual Meeting of the EBMT in Geneva, Switzerland, there are two Question & Answer sessions being organised for both the CALM and the Plerixafor Off-label Transplant Use (see below) studies. This will be an opportunity for data managers and physicians to ask questions about the data entry and to meet the study coordinators:

Marcha Suits  Annelies Kleijne

- Monday 2 April 13.05 – 13.45h
- Tuesday 3 April 12.10 – 13.00h

The location will be the Data Management Sessions room. It is also possible to make an individual appointment with the study coordinators.

Plerixafor Off-label Transplant Use Study (Non-Interventional Prospective Study)

As a post-marketing commitment, Genzyme is required to monitor the off-label transplant use of plerixafor. The off-label use of plerixafor will be collected over a 5 year time span, between 31 July 2009 and 31 July 2014. The EBMT registry will be used to fulfil this commitment.

Eligible for the study are patients treated with plerixafor who have one or more of the following:

- Background disease other than lymphoma or multiple myeloma
- Are younger than 18 years of age
- Received transplant using ex vivo plerixafor-mobilised cells (umbilical cord cell, peripheral blood, bone marrow cell collection)
- Received treatment with plerixafor alone (i.e., without granulocyte colony stimulating factor (G-CSF))
- Contra-indication for G-CSF
- Transplants using plerixafor-mobilised cells from allogeneic donor
- Received transplant using plerixafor-mobilised bone marrow cells
- Routes of plerixafor administration other than subcutaneous
- Patients whose cells do not mobilise poorly
- Other

The data request for this study has been kept to an absolute minimum. Centers are asked to complete a short 2-page MED-C form which collects the off-label transplant use indication and patient identification items. EBMT expects the MED-A data forms to be registered at day 100 after transplant as usual.

At present 210 EBMT centers have been invited to participate, more invitations will be sent shortly. Eight centers have registered for participation, expecting to provide data on more than 70 transplants in total. Eleven patients have been included in the study so far. To get more insight in the off-label transplant use of plerixafor and for reporting this to the EMA as requested, it is important that as much data as possible...
are being collected. Therefore every center is welcome to participate and contribute to the collection of any plerixafor off-label transplant use. For more information about the study or registration, please have a look at the EBMT website or contact study coordinator Annelies Kleijne at the EBMT Data Office in Leiden via e-mail address: plerOLebmt@lumc.nl.

A Non-Interventional Prospective Study on the Effect of Transfusions and Iron Toxicity in untreated adult patients with Myelodysplastic Syndrome (MDS) or Chronic Myelomonocytic Leukemia (CMML) treated with Reduced Intensity and Myeloablative Allogeneic Stem Cell Transplantation (allo-SCT)

The MDS subcommittee of the Chronic Leukaemia Working Party (MDS-CLWP) is conducting a study to prospectively evaluate the effect of iron toxicity on treatment outcome after myeloablative (MAC) and reduced intensity (RIC) allogeneic SCT, in previously untreated adults with high risk MDS.

Allogeneic Stem Cell Transplantation (alloSCT) and blood product transfusions are standard care for Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic leukemia (CMML). Several studies have shown remarkable changes in serum ferritin and non-transferrin-bound iron (NTBI) in patients undergoing allo-SCT. A relevant proportion of MDS patients are at risk for organ damage due to the development of iron overload. Iron chelation therapy may reduce the acute and chronic treatment-related toxicity by removing excess of iron, iron radicals and reactive oxygen species (ROS). However, little information is available about the efficacy and safety of iron chelation in MDS and CMML patients.

A retrospective study on Iron Toxicity in MDS patients shows interesting and promising findings, yet limited data are available. Therefore we developed a non-interventional prospective study on iron toxicity. This study evaluates the effect of iron toxicity on treatment-related mortality in adult MDS/CMML patients during and after treatment with Myeloablative Conditioning (MAC) and Reduced Intensity Conditioning (RIC) allogeneic hematopoietic stem cell transplantation (allo-HSCT) without prior intensive antileukemic therapy.

The patient inclusion criteria are:

All adult MDS/CMML patients during and after treatment with Myeloablative Conditioning (MAC) and Reduced Intensity Conditioning (RIC) allogeneic hematopoietic stem cell transplantation (allo-HSCT) without prior intensive antileukemic therapy.

Patients may be included retrospectively from the start of the study at 01-11-2009. Because we have obtained an educational grant for this study, we can reimburse you 500€ per fully evaluable patient.

We are happy to report that at this moment 43 centres have signed up for participation, and 144 patients have already been included in the study. For a meaningful analysis, 200 patients are needed in this prospective non-interventional study.

The registry will include patients from 01-11-2009 to 31-07-2012 with 2 years of follow up.

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A Non-Interventional Prospective Study to Evaluate the Effect of Prior Therapy with Nilotinib or Dasatinib on the Outcome after Allogeneic SCT for Patients with Chronic Myeloid Leukemia.

The CML subcommittee of the Chronic Leukaemia Working Party (CML-CLWP) is conducting a study to evaluate the effect of prior therapy with Nilotinib or Dasatinib on the outcome after allogeneic stem cell transplantation for adult patients with Chronic Myeloid Leukemia.

While the use of Imatinib prior to stem cell transplantation seems to have no adverse impact on the outcome of allogeneic stem cell transplantation little is known on the impact of prior use of second generation TK inhibitors. Therefore this non-interventional prospective study addresses this question and patients undergoing allogeneic stem cell transplantation after prior use of 2nd generation TKIs will be followed by the EBMT Leiden office on engraftment, treatment related mortality, relapse rate and survival, prospectively. Details on TKI therapy will be collected by the participating centres, retrospectively.

There is no upper limit to the number of patients entered, but it is estimated that up to 400 patients will be included in this prospective non-interventional study.

The registry will include patients from 01-01-2010 to 31-12-2013 with 2 years of follow up.

The patient inclusion criteria are:

All adult patients with chronic myeloid leukemia in any phase (chronic, accelerated or blastic) who undergo any type of allogeneic stem cell transplantation and have been previously treated with Nilotinib or Dasatinib, regardless of their response to this TKI.

Patients may be included retrospectively from the start of the study at 01-01-2010.

We are happy to report that at this moment 69 centres have signed up for participation, and 173 patients have already been included in the study.
Disease status at HSCT:

Division by age and donor:

For more information about the non-interventional study on 2nd generation TKI, please have a look at the EBMT website or contact study coordinator Jennifer Hoek at the EBMT Data Office in Leiden via e-mail address: clwpebmt@lumc.nl or j.d.c.hoek@lumc.nl

This study is running according to a fixed time-schedule. The first milestone was reached at the end of 2011, when 150 patients were included.

**Our next milestone is set at the end of 2012, at which date we want to have received all data up to and including the 1 year follow up for the patients with study numbers 1-150.** The graph below shows that we are almost halfway, **so please plan ahead and reserve time this year to update your patients in this study.**
Q&A session next EBMT Annual Meeting in Geneva!

At the 38th Annual Meeting of the EBMT in Geneva, Switzerland, a Question & Answer session is being organised for several EBMT studies, including the non-interventional study on 2nd generation TKI. This will be an opportunity for data managers and physicians to ask questions about data entry for this study and to meet the study coordinator:

- Monday 2 April 13.05 – 13.45h

The location will be the Data Management Sessions room. Naturally, it is also possible to make an individual appointment with the study coordinator via e-mail address j.d.c.hoek@lumc.nl