One of the largest haematology congresses was this year organized in the beautiful city of Barcelona, Spain. There were about 8500 delegates from all over the world. Only the congress of the American Society of Hematology is bigger: about 25,000 delegates. This congress is every year in December in the U.S.A.

The delegates are medical doctors, scientists, analysts and oncology nurses. I am allowed by the Dutch Contact Group for Leukaemia patients to join this European congress.

There are many simultaneous presentations, plenary sessions, poster presentations, etc. on every subject regarding haematology: coagulation, inheritable blood diseases, malicious blood diseases (like leukaemia), lymphoma’s etc. I concentrated on leukaemias.

On this congress there are always exhibitions of the pharmaceutical companies, who try to promote their drugs.

The highlights on leukaemia on this congress were leukaemic stem cells (and irradiation of them) and epigenetic treatments; this means trying to influence methylating of DNA and acetylating of histone proteins.

**Chronic myeloid leukaemia (CML) presentations:** The results of a study of the efficacy of dasatinib over longer time in comparison with imatinib was presented. From the results it appeared that dasatinib as first treatment choice in nearly all respects was better than imatinib. An earlier complete cytogenic response was reached or even a complete molecular response! There was less progression of the disease to accelerated phase or blast crisis. Failing of treatment or resistance were also less. Moreover side effects were also less than for imatinib, except for pleural effusion, which has to be watched for.

Exact the same was found in a comparable study over longer time for nilotinib and imatinib. Nilotinib did better in all respects than imatinib (see here above). Only a comparison between nilotinib and dasatinib has to be made!

One of the side effects of dasatinib is that relatively much patients (54%) have problems with pleural effusion. In a study one tries to decrease this to 20% by very carefully attending the dose by the concentration of the drug in the blood.

With CML there is a translocation between chromosomes 9 and 22, which implies that a fusion gene, the BCR/ABL gene is generated, which results in a fusion protein which forces the cells in continuous division. The last time one asks oneself if there are more genetic aberrations with CML. This is important. Because with disregulation of other genes, maybe other entries can be found for killing leukaemic stem cells with other means than tyroine kinase inhibitors imatinib or nilotinib or dasatinib. It appears that in CML cells the gene CXCR4 is less present than in normal cells. The protein CRCX4 has to do with apoptosis (regulated self killing) of healthy, normal cells. In CML cells this protein is less present. Imatinib takes care that the CRCX4 protein in leukemic CML cells is present in normal quantities and that these cells die.

Plerixafor is a substance, that prevents that leukaemic CML cells do not undergo apoptosis. If one can find a substance that inhibits plerixafor, than possibly CML stem cells can undergo apoptosis.
Some time ago bosutinib has been called as a possible agent against CML. Bosutinib has now been used in a trial with patients who are intolerant or resistant against imatinib. From this study it appeared that bosutinib works with these patients, only not with those who have the T315I mutation.

For CML patients with the T315I mutation there is no treatment other than stem cell transplantation or treatment with homoharringtonine is available. The BCR/ABL protein with these patients can not bind imatinib, dasatinib, nilotinib or bosutinib.

A very interesting investigation was the study for differences between normal and leukaemic stemcells. It appeared that there is one difference in surface proteins between these two cell types. No wit may be possible to develop an antibody against this protein on the leukaemic stemcells. From this antibody a vaccin can be made. Probably the development of such a vaccin is will take a long time.

Completely new during this congress was that there was a session devoted to patient – research contact. Jan Geisler already made a report on this item.

During the EHA congress much attention was payed to the epigenetic changes in DNA. This means, that there are non-inheritable changes in DNA, which can make a malicious cell from a normal cell. A direct connection between these epigenetic changes and CML is not (yet) shown. However, as it has been shown that there are more genetic changes in CML than the BCR / ABL translocation only, it may appear that other changes than BCR / ABL have to do with these epigenetic changes. As this becomes true, it opens up new possibilities for treatment.

Epigenetic processes are (among others): methylation of DNA and acetylation and methylation of histon proteins. So it is known, that the gene TET2 has to do with the methylation of DNA. The methylated parts of the DNA are less admissable for transcription. This means, that no RNA is made from these methylated genes and so there is no protein made of the genes. This can influence the cell division: The cell can continuously divide and therefore has changed in a malicious cell. This way in which a normal cell changes into a malicious cell is called epigenetic change.

The gene EZH2 also codes for a certain protein which regulates the methylation and acetylation of histones. The histones are proteins that form a complex with DNA and methylation and acetylation that the complex between DNA and histones is a loose complex. On the other hand, demethylation and deacetylation of histones makes that DNA and the sproteins form a very tight complex, which prevents making of RNA from the DNA. The EZH2 protein acetylates histones and thus promotes forming of RNA. It even can happen that too much of certain proteins is made: A disregulation of the life of a cell; it can eventually turn into a cancer cell.

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