# HLA – oriented therapy for gastric cancer.
# A novel approach therapy

Roxana SISU, MD

Cardiology Department, Emergency University Hospital, Bucharest, Romania

Alterations in gene and protein expression have been reported to predict response to several cancer therapies. However it is an exciting field of research, it has not yet been applied routinely in clinical practice.

Human leukocyte antigens (HLA) are glycoproteins found on the surface membrane of cell in the body. Their main function is to help the immune system defend against cancers, bacteria, viruses, and parasites.

Taking in consider different types of HLA antigens, there have been several reports on responses to therapy, but the number of cases has been insufficient.

To the best of our knowledge, this is a novel approach in cancer treatment territory.

The aim of this study was to evaluate, by using a retrospective and a prospective one, whether the HLA antigen classification would have a clinical benefit for patients.

The retrospective study consisted of a consecutive series of 1932 Japanese patients with histologicaly confirmed gastric adeno-carcinoma who underwent gastrectomy from Jan.1977 to May 1996. The prospective study consisted of a 582 patients with the same types of cancer from Jun.1996 to Aug. 2005. Clinical data was obtained from the database of the Japanese Society of Strategies for Cancer Research and Therapy.

HLA antigens were serologically tested for HLA-A, B, C, DR, and DQ antigens. According to the incidence of HLA antigens, these patients were retrospectively classified in the retrospective study into four groups. HLA type II patients were characterized by HLA-A3, -A33, -B12, B13, and – DR6; Type III by HLA-B46, - B54, -B55, -b56, -Cw1, -DR4, and – DQ4; type IV by HLA – B7, - B16, Cw7, and-DR1, and the rest were type I, a common type in Japan. The HLA antigens were examined in gastric cancer patients before surgery and the evaluation of the surgical outcomes were done according to the HLA classification.

The therapies consisted of gastrectomy alone, a chemotherapy group and an immunotherapy group. The chemotherapy group received gastrectomy with fluoropyrimidines/mitomicyin C or both. The immunotherapy group received gastrectomy plus PSK – a polysaccharide comp-lex with immune stimulating effects, derived from the mushroom Coriolus Versicolor, or a combination between PSK and a chemotherapic agent. In the retrospective study patients were followed over 10-years after treatment and over 5 years after treatment in the prospective study. There were no significant differences in each

group in gender, TNM stages, histology, and types of gastrectomy.

The retrospective study showed that the patients with HLA type I, II, and IV had good outcomes if they were treated with immunotherapy, and those with HLA type III had good outcomes if treated with chemotherapy.

On the basis of these data, the authors conducted the prospective study in accordance with patients' HLA classification as HLA-oriented therapy. The original idea of the present study was that a patient, who had a similar genomic signature, might obtain a good outcome if he received similar therapy. The results were similar to the retrospective study.

This study also found correlations between specific patterns of HLA antigens and metastasis and secondary cancer.

In conclusion, this study showed an important clinical impact of determining HLA antigens preoperatively. It also showed that HLA-oriented therapy, particularly the immuno-modulation therapy, is a promising field in the treatment of gastric adenocarcinoma.

---