Prognostic Significance of Immune Checkpoint Molecule Expression in Resectable Gastric Adenocarcinoma

Vlad M. Croitoru[1], Alexandru Filippi[1], Irina M. Cazacu[1], Shuji Kitahara[2], Aya Matsui[2], Gregory Lauwers[2], Andrei Sorop[1], Laura Georgiana Necula[3], Lilia Matei[3], Catalin Pechianu[1], Adina Croitoru[1], Vlad Herlea[1], Adrian Saftoiu[4], Mihaela Chivu-Economescu[3], Simona Olimpia Dima[1], Dan Duda[2] and Irinel Popescu[1]

1 Fundeni Clinical Institute, Center of Excellence in Translational Medicine, Bucharest, Romania
2 Edwin L. Steele Laboratories for Tumor Biology, Department of Radiation Oncology, Massachusetts General Hospital, Boston, Massachusetts, USA.
3 Stefan S Nicolau Institute of Virology, Cellular and Molecular Pathology Dep., Bucharest, Romania
4 Research Center of Gastroenterology and Hepatology University of Medicine and Pharmacy Craiova, Romania

Background

Survival rates of gastric cancer remain poor and, hence, there is a great need to identify novel treatment strategies and relevant predictive and prognostic biomarkers.

Immunotherapies targeting the PD-1/PD-L1 checkpoints have shown promising results, but simultaneous inhibition of other immune checkpoint molecules may further improve clinical outcome.

The expression and prognostic significance of other immune checkpoint molecules have not been extensively explored, especially among resectable gastric cancer patients.

Herein, we prospectively examined the expression of several immune checkpoints and their correlation with survival in patients with resectable gastric cancer.

Methods

39 patients who underwent curative surgery for gastric adenocarcinoma at Fundeni Clinical Institute were included in this study. The expression patterns of several immune checkpoints were examined on immune cells using Luminex xMAP technology with ProcartaPlex Human Immuno-Oncology Checkpoint Marker panel 14-plex from tumoral and peritumoral resected specimens.
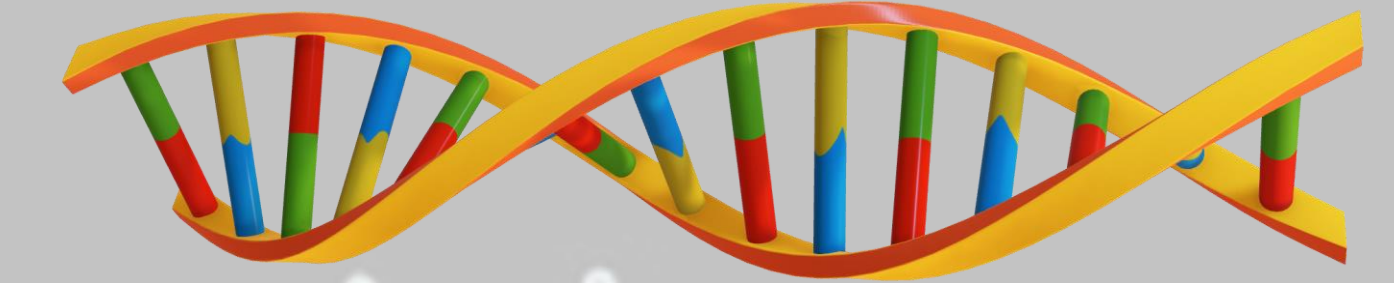
ProcartaPlex Human Immuno-Oncology Checkpoint Marker panel 14-plex (Thermo):

Stimulatory molecules: CD27, CD28, CD137 (4-1BB), GITR, HVEM
Inhibitory molecules: BTLA, CD80, CD152 (CTLA4), IDO, LAG-3, PD-1, PD-L1, PD-L2, TIM-3.
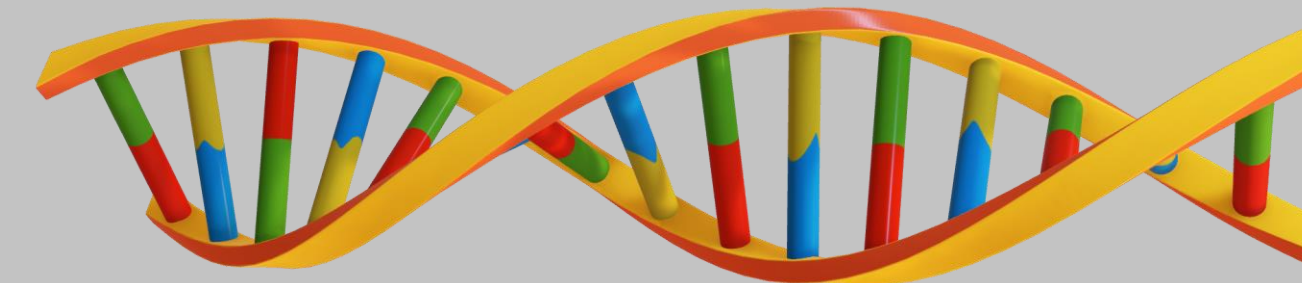
Results

Inhibitory immune checkpoints proteins CD80 and BTLA showed significant increase in tumor samples comparing with peritumoral control samples

Inhibitory immune checkpoints proteins TIM3, CTLA4, LAG3 showed a slight increase in tumor samples comparing with peritumoral control samples

Increased LAG-3 and GITR expression in primary tumors were independent factors for prolonged overall survival (p=0.02 and p=0.008, respectively)

Conversely, ICOS was associated with shorter overall survival (p=0.04)

Moreover, ICOS expression in primary tumors was significantly associated with PD-1 expression while GITR expression was positively correlated with TIM-3

No statistically significant association was found between the other immune checkpoint molecules and survival
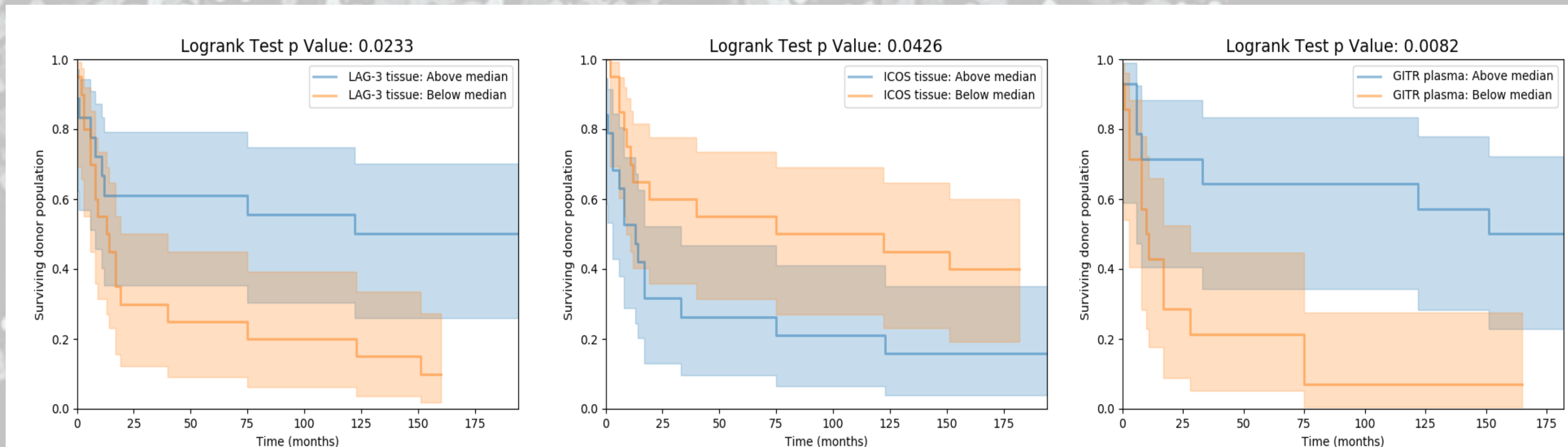
Conclusion

Our results indicate that increased expression levels of LAG-3, GITS and ICOS are independent prognostic factors for overall survival in patients with curatively resected gastric cancer. These immune checkpoint molecules should be further evaluated as novel predictive and/or therapeutic targets for gastric cancer patients.

Poster 37P
Presenting author: Croitoru M. Vlad
Email: vlad.m.croitoru@gmail.com