Validation of A New Scoring System for Molecular Subtyping of Gastric Cancer

Irina M. Cazacu1, Alexandru Filippi1, Vlad M. Croitoru1, Shuji Kitahara2, Aya Matsui2, Gregory Lauwers2, Andrei Sorop1, Laura G. Necula1, Lilia Matei1, Catalin Pechianu1, Adina E. Croitoru1, Vlad Herlea1, Adrian Saftoiu1, Doru Pau1, Mihaela Chivu-Economescu1, Simona Dima1, Dan G. Duda1, Irinel Popescu1

1. Funeni Clinical Institute, 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, Craiova, Romania
5. Weill Cornell Medical Center, New York, USA.

Background
Molecular classification of gastric cancer may potentially provide tailored treatment options by predicting survival outcomes and patients' response to therapy. In our prior study by Setia et al.*, we identified five groups of gastric cancers based on Epstein–Barr virus (EBV) positivity, microsatellite instability, aberrant E-cadherin, and p53 expression (normal/aberrant). The aim of this study was to validate the relationship between these molecular subtypes and prognosis of patients with gastric cancer from Romania.

Methods
The molecular classification was reproduced in a retrospective cohort of 122 resected gastric cancers at Funeni Clinical Institute, Bucharest. The patients were classified in 5 subtypes based on the expression of 14 different biomarkers: Epstein-Barr encoding region (EBER) in situ hybridization for EBV detection, MSI (microsatellite instability) status (MSI Analysis System, Promega Inc), and immunohistochemistry (IHC) for E-cadherin, p53 and MUC6.

Results

Gastric cancers – Romanian retrospective lot - 122 samples

Molecular subtypes and survival

Data analysis indicated a favourable prognostic role for microsatellite instability high group (MSI-high – Gp2) vs Gp3 (Gastric cancers with aberrant E-cadherin expression), Gp 4 (Gastric cancers with aberrant p53 expression) and Gp 5 (Gastric cancers with normal p53 expression) in resectable gastric cancer.

Conclusions
Patient stratification using the proposed molecular classification successfully stratified associated with differential overall survival. Our results demonstrated a trend for superior survival in the microsatellite-instable subtype and EBV positive gastric adenocarcinomas.