**Response to biologics in IBD patients assessed by Computerized image analysis of Probe Based Confocal Laser Endomicroscopy with molecular labeling**

**Authors: Iacucci M1\*, Grisan E2\*, Labarile N1, Nardone O1, Smith SCL1, Jeffery L1, Cannatelli R1, Ghosh S1, Buda A3**

1. Institute Translational of Medicine, Institute of Immunology and Immunotherapy and NIHR Birmingham Biomedical Research Centre, University Hospitals NHS Foundation Trust and University of Birmingham, Birmingham, UK
2. School of Engineering, London South Bank University, London SE1 0AA, UK
3. Department of Gastrointestinal Oncological Surgery, S. Maria del Prato Hospital, Feltre, Italy

\* The authors contributed equally to the research.

**Background**

The increase in therapeutic choices in inflammatory bowel diseases (IBD) imposed the identification of personalized therapeutic strategy. Confocal laser endomicroscopy (CLE) is a new endoscopic tool developed to obtain virtual in vivo histology. This study aimed to identify CLE *in vivo* and *ex vivo* features predictive of response for patients starting biologics.

**Methods**

We performed a prospective observational study: 29 patients (14 ulcerative colitis-UC and 15 Crohn’s Disease-CD) underwent CLE before and after biological treatment. CLE parameters analyzed were: crypt distribution, crypt area (CA), eccentricity, diameter, inter-cryptic distance (ICD), vessel tortuosity (VT), fluorescein leakage through the colonic mucosa (FLCM) and ex-vivo binding activity of fluorescein-labelled biologics on biopsies. Mosaicism of CLE images were analyzed using a dedicated software algorithm (CellvizioViewer, Mauna-Kea-Technologies, Paris-France). A Graphical User Interface was designed for a semiautomated analysis.

**Results**

After treatment, VT changed in overall population; FLCM decreased in UC patients, whilst CA, eccentricity and ICD in CD patients (p< 0.05). FLCM was the best parameter for predicting responsiveness (AUROC 83%, accuracy 83%, PPV 94% and NPV 57%). FLCM and ICD were the best discriminants in responders Vs non-responders in UC (AUROC85%, accuracy 85%, PPV 100% and NPV 71%); whilst VT, CA and ICD in CD (AUROC 95%-86%-83%; accuracy 90%-90%-88%; PPV 100%-100%-86%; and NPV 75%-75%-100%, respectively). UC patients, but not CD patients, had higher basal fluorescent intensity signals with a significant reduction after treatment (p< 0.05). An increased mucosal binding to the fluorescent labelled biological agent was associated to a higher likelihood of therapy response (AUROC 81%-64%, accuracy 77%-79%, PPV 100%-80%, NPV 63%-50% in UC and CD patients respectively).

**Conclusion**

FLCM and ICD were the best discriminants of response in UC, while VT, CA and ICD in CD. A higher mucosal binding to a biological agent before treatment was observed in responders UC patients but not in CD patients.