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

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**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.