72.9%] vs 65.0% [95%CI=58.3−70.9%]; uHR=0.77 [95%CI=0.60-0.98], *P*=0.035 and aHR=0.81 [95%CI=0.63-1.03], *P*=0.083).Adding Immunoscore to a model containing all clinical variables significantly improved prediction of DFS (likelihood ratio test, *P*<0.001).

Conclusions: This study confirms the prognostic value of IS in patients with stage III CRC treated with CAPOX or FOLFOX and suggests that IS low cases may gain greater benefit from receiving CAPOX than FOLFOX. Validation of this result is merited.

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337P Prediction of poor response to oxaliplatin by an RNA signature derived and validated in colorectal cancer clinical trials

S. Hassanieh[1], E. Domingo[1], A. Blake[1], D. Fisher[2], K.L. Redmond[3], S.D. Richman[4], S.M. Walker[5], P. Quirke[4], R.H. Wilson[6], R. Kennedy[3], I. Tomlinson[7], R.S. Kaplan[2], L. brown[2], P. Dunne[3], M.T. Seymour[4], D. Morton[8], R.A. Adams[9], N. West[4], T. Maughan[1]

[1]Department of Oncology, University of Oxford, Oxford, UK; [2]Medical Research Council Clinical Trials Unit, University College London, London, UK; [3]Patrick G Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, UK; [4]Leeds Institute of Cancer and Pathology, St. James's University Hospital, Leeds, UK; [5]Internal Products, Almac Diagnostics, Craigavon, UK; [6]Institute of Cancer Sciences, University of Glasgow, Glasgow, UK; [7]Cancer Research UK Centre, University of Edinburgh, Edinburgh, UK; [8]Department of Surgery, University of Birmingham, Birmingham, UK; [9]School of Medicine, Cardiff University, Cardiff, UK

Background: Colorectal cancer (CRC) is usually treated with oxaliplatin-based regimens in stages II, III and IV as standard of care. However, no predictive oxaliplatin biomarker has ever been fully validated despite intensive research. Here we aimed to discover a biomarker of early progression on oxaliplatin based chemotherapy with potential use in the clinic to guide therapy selection.

Methods: The COIN clinical trial was used as a discovery set selecting patients either on continuous or intermittent fluoropyrimidine chemotherapy combined with oxaliplatin. 3'RNAseq was successfully applied to primary CRCs from patients either progressing within the first 12 weeks (progressors, n=47) or progressing after 18 weeks (non-progressors, n=112). Validation was performed on two clinical trials profiled with Almac XCel microarray by the S:CORT consortium: FOCUS (N=359) and FOxTROT (N=93). The former is composed of stage IV CRCs randomised for 5FU/FA with or without oxaliplatin and the latter of high risk stage II and III CRCs treated with neoadjuvant FOLFOX.

Results: Analysis on COIN identified 29 differentially expressed genes comprising the new RNA signature. In the randomized FOCUS trial, this signature used as a continuous score in patients treated with single agent 5FU/FA (76 poor responders/211 good responders) did not show any signal (OR=1.09 (0.51-2.35), P=0.82). The FOLFOX arm was statistically underpowered (7 poor responders/67 good responders) but did show a trend in the expected direction (OR=3.25 (0.38-27.72), P=0.28) where the interaction with the 5FU/FA arm was not significant (OR=2.84 (0.14-57.07), P=0.49). In FOxTROT, using the endpoint pathological response post-treatment (69 progressors/24 non-progressors), the signature was significantly associated with poor response (OR=3.31 (1.03-10.60), P=0.04).

Conclusions: A new RNA signature has been generated and validated in high quality clinical trial CRC data identifying patients with early progression on oxaliplatin + 5FU/FA. Despite heterogeneity in the clinical settings used, this signature has the potential to provide useful information for oxaliplatin stratification in future clinical trials.

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338P A new clinically applicable immune-metabolic signature (IMMETCOLS) reveals metabolic singularities in consensus molecular subtypes (CMS) in colorectal cancer

S. Madurga[1], C. Foguet[2], H. Oliveres[3], F. Mas[1], J. Maurel[3], M. Cascante[4]

[1]Department of Material Science and Physical Chemistry, Universitat de Barcelona, Barcelona, Spain; [2]Faculty of Biology, Department of Biochemistry and Molecular Biomedicine & Institute of Biomedicine of Universitat de Barcelona, Barcelona, Spain; [3]Medical Oncology, Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [4]Department of Biochemistry and Molecular Biomedicine, Institute of Biomedicine of Universitat de Barcelona (IBUB), Barcelona, Spain

Background: In the last years, a great effort has been made to unify different independent colorectal cancer (CRC) molecular classification systems into four consensus molecular subtypes (CMS). The four subtypes are found to be associated with distinct microenvironmental features and clinical outcome, although metabolic singularities are not well established. Metabolic dysregulation has been reported as a hallmark of CMS3 but metabolic heterogeneity among other subtypes has not been investigated. Here, taking into account the increasing evidence on the importance, for determining response to therapies, of the metabolic crosstalk between cancer cells, tumor microenvironment and immune cells, we investigated the metabolic singularities in the four CMS using a genetic immune-metabolic signature (IMMETCOLS).

Methods: We evaluated the correlation of CMS signature using CMS classifier with single sample predictor (SSP) and the new IMMETCOLS signature (10-gene expression classifier) that separates three clusters; IMC1: Mesenchymal high glycolytic/low Oxphos, IMC2: Epithelial low glycolytic/high Oxphos and IMC3: Epithelial high glycolytic/high Oxphos, in two public data sets (TCGA, n=512 patients and GES, n=1328 patients). CMS and IMMETCOLS interactions with overall survival were also analyzed.

Results: IMMETCOLS clusters (ICM1-33%, ICM2-14%, IMC3-53%) and CMS subtypes (CMS1-24%, CMS2-44%, CMS3-14%, CMS4-18%) are distributed as previously published. CMS1 is characterized by a mixture of IMC1 (47%) and IMC3 (47%) and CMS4 is basically constituted by IMC1 (90%). Finally, CMS2 and CMS3 subtypes are mainly distributed in IMC3 (71%) and IMC2 clusters (22%). Either CMS4 and IMC1 confers poor prognostic. Importantly, our data demonstrated that ICM2 has the worst overall survival in the CMS2 subtype.

Conclusions: IMMETCOLS signature refines CMS prognosis in CRC patients and potentially allows specific metabolic interventions in CMS subtypes.

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339P Molecular subtyping for chemotherapy response prediction in early stage colon cancer

S. van de Weerd[1], A. Torang[1], M. Smit[2], I. van den Berg[3], J. Roelands[2], W. Mesker[2], D. Bedognetti[4], P. Kuppen[2], H. Putter[5], R.A.E.M. Tollenaar[2], W.R.L. Hendrickx[4], C. Jimenez[6], G. Vink[7], M. Koopman[7], J. Roodhart[7], J. Ijzermans[3], H. van Krieken[8], J-P. Medema[1]

[1]Center for Experimental and Molecular Medicine, Amsterdam University Medical Center (UMC) - locatie Academic Medical Center (AMC), Amsterdam, Netherlands; [2]Department of Surgery, LUMC-Leiden University Medical Center, Leiden, Netherlands; [3]Department of Surgery, Erasmus MC - Erasmus University Rotterdam, Rotterdam, Netherlands; [4]Immunology Inflammation and Metabolism Department, Sidra Medical and Research Center, Al-Rayyan, Qatar; [5]Medical Statistics, LUMC-Leiden University Medical Center, Leiden, Netherlands; [6]Medical Oncology, Amsterdam UMC - Vrije University Medical Centre (VUmc), Amsterdam, Netherlands; [7]Medical Oncology Department, UMC - University Medical Center Utrecht, Utrecht, Netherlands; [8]Department of Pathology, Radboud University Medical Center, Nijmegen, Netherlands

Background: Biomarkers that can predict chemotherapy response are much needed to improve and tailor treatment strategies in early stage colon cancer (CC). The consensus molecular subtype (CMS) classification divides CC in four biologically distinct subtypes and holds great promise as a predictive biomarker. To realize implementation into clinical practice, robust classification methods are needed and additional data is warranted on the predictive value of CMS for therapy response.

Methods: Two CMS identification methods were evaluated. First, we analysed the association between four histopathologic markers (tumour infiltrating lymphocytes (TILs), amount of mucus, tumour stroma ratio (TSR) and tumour budding) and CMSs in 218 early stage CC patients with available RNA-based CMS labels. Second, we generated NanoString and RNA sequencing profiles of 28 paired fresh frozen (FF) and formalin-fixed paraffin-embedded (FFPE) CC samples, plus 168 FF samples from an additional CC cohort, in order to develop a NanoString classifier. The gold standard CMS classifier was used as reference.