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Leveraging artificial intelligence to predict immune checkpoint inhibitor (ICI) efficacy in proficient MMR mCRC: Translational analyses of AtezoTRIBE and AVETRIC trials

M. Carullo[1], C. Antoniotti[1], C. Ahn[2], C. Oum[2], V. Angerilli[3], F. Bergamo[4], C. Sciortino[5], A. Boccaccino[6], M.A. Calegari[7], J. Gasparello[8], S. Tamberi[9], R. Intini[4], M. Scartozzi[10], C. Damonte[5], C. Citterio[11], L. Salvatore[7], C. Boccaccio[1], M. Fassan[12], C-Y. Ock[2], C. Cremolini[1]

[1] Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy, [2] Oncology Group, Medical Affairs, Lunit, Seoul, Republic of Korea, [3] Surgical Pathology Unit, ULSS2 Marca Trevigiana, Treviso, Italy, [4] Oncology 1 Unit, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy, [5] Department of Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, [6] Oncology Department, Ospedale Santa Maria delle Croci, Ravenna, Italy, [7] Dipartimento di Oncologia, Università Cattolica del Sacro Cuore and Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS Rome, Rome, Italy, [8] Department of Medicine, Università di Padova, Padua, Italy, [9] Department of Medical Sciences (DIMEC), University of Bologna, Ospedale Santa Maria delle Croci, AUSL Romagna, Ravenna, Italy, [10] Medical Oncology Department, University of Cagliari, Cagliari, Italy, [11] Department of Quality and Safety, Unit of Innovation, Research and Quality, Azienda USL di Piacenza, Piacenza, Italy[12] Biomedical Laboratory Techniques School of Medicine and Surgery, University of Padua, Department of Pathology Ca' Foncello Hospital, ULSS2 Marca Trevigiana, Treviso, Italy

Background

Artificial Intelligence (AI) methods may enable to extract predictive biomarkers from tumor hematoxylin & eosin (H&E) whole-slide images (WSIs). We aimed to develop an AI-driven biomarker predictive of ICIs benefit in proficient mismatch repair (pMMR) metastatic colorectal cancer (mCRC) using Lunit SCOPE IO platform.

Methods

Lunit SCOPE IO quantified the density of lymphocytes (LC), fibroblasts (FB), macrophages (MP), tumor (TC), endothelial (EC) and mitotic (MTC) cells in cancer area (CA) and stroma (CS) on pre-treatment H&E WSIs from pts with pMMR mCRC enrolled in AtezoTRIBE (FOLFOXIRI/bevacizumab +/- atezolizumab [atezo]) and AVETRIC (FOLFOXIRI/cetuximab/avelumab) trials. A multivariate Cox regression model was trained using the most predictive variables for progression-free survival (PFS; average C-index > .5) in the AtezoTRIBE atezo-treated arm. A PFS-based cut-off set by maximal rank statistics dichotomized tumors as biomarker-*high* or *low*. AVETRIC served as a *validation set*.

Results

The AI-driven analysis of WSIs from 161 patients (pts) enrolled in the AtezoTRIBE study identified a biomarker incorporating densities of TC, MTS, LC on CA and FB, MP, EC on CS. Among them,113 (70%) pts were classified as biomarker-*high*, characterized by older age (*P*=.030) and higher incidence of liver metastases (*P*= .023). In atezo arm, biomarker-*high* pts had better prognosis as compared to biomarker-*low* pts (PFS *P*= .036, Overall Survival [OS] *P*= .024), but not in control arm (PFS *P*= .564, OS *P*= .186). Interactions between treatment and biomarker were found in PFS (*P*=.114) and OS (*P*= .025), with biomarker-*high* pts but not biomarker-*low* ones deriving benefit from adding atezo (*high*, HR PFS: 0.69, 95%CI 0.45-1.04; OS: 0.54, 95% CI 0.33-0.88; *low*, HR PFS: 1.34, 95%CI 0.66-2.72; OS: 1.70, 95% CI 0.69-4.20). In the AVETRIC cohort, WSIs from 48 pts were analyzed; 36 (75%) cases were classified as biomarker-*high*, with better PFS (*P*= .043) and OS (*P*= .053) compared to biomarker-*low* ones.

Conclusions

Our AI-derived tumour microenvironment biomarker may help to predict benefit from ICI-based treatments in pMMR mCRC, supporting further investigations of AI-powered approaches.

Clinical trial identification

AtezoTRIBE: NCT03721653; AVETRIC: NCT04513951.

Legal entity responsible for the study

GONO Foundation.

Funding

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Disclosure

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