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Development and validation of a predictive score to identify K-Ras wild-type (WT) metastatic colorectal cancer (mCRC) patients who are likely to benefit from Panitumumab (P) treatment.

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Background: Practice guidelines recommend using P to treat K-Ras WT mCRC patients where it was shown to significantly extend overall survival (OS). Still, a proportion of patients will not achieve this goal. We propose a simplified predictive score to identify patients who are likely to benefit from P treatment. **Methods:** NCT00364013 was used as training dataset (TRS) (n = 460) with NCT00339183 (TES1) (n = 479) and NCT00113763 (TES2) (n = 191) as validations sets. Datasets were obtained from www.projectdatasphere.org and included K-Ras WT mCRC patients treated with P in combination or not with FOLFOX4 (FOL) or FOLFIRI as 1st, 2nd, or 3rd line therapy. TRS was used to generate synthetic representations (SRs) for each patient through the integration of 36 clinical and analytical features collected, respectively, during the screening phase and the first month of inclusion. These SRs were then input into a deep learning framework (DLF) to identify subgroup of patients based on their similarities. The resultant subpopulations were correlated with OS. Differential variables between subgroups were identified through feature contribution analysis and included in a multivariable logistic regression model. Independent predictive factors found to be statistically significant were used to generate a predictive score of P response at baseline that was validated in the test sets. **Results:** DLF identified two different subpopulations: SPA (n = 162) and SPB (n = 298). Patients in SPA had a lower risk of death when treated with P/FOL compared to FOL (HR 0.68 95%CI 0.48-0.99; p = 0.04). Patients in SPB showed no significant differences between P/FOL and FOL (p = 0.27). Feature contribution analysis identified 15 differential features between both subpopulations. From these, CEA > 174 ng/ml, ALP > 131 IU, LDH > 703 IU, and platelets > 374 10^9/L were selected to create a simplified predictive score for P response ranging 0-18 (if > than the depicted values: 6.5 points for CEA, 5.5 for LDH, and 3 points for each other characteristic). When applied to TRS, this score yielded an area under the curve of 0.87 (95%CI: 0.84-0.91). A score ≥8.5 was positively correlated to a longer OS after P/FOL compared to FOL (HR 0.65 95%CI 0.43-0.98; p = .04). No significant differences were observed between P/FOL and FOL in patients with a score < 8.5 (p = 0.89). The predictive score was then validated in the two test sets with similar results (score ≥8.5, TES1: HR 0.59 95%CI 0.40-0.88 p = .009; TES2: HR: HR 0.58 95%CI 0.35-0.96 p = .03; score < 8.5, TES1: p = .5; TES2: p = .1). **Conclusions:** Based on CEA, ALP, LDH and platelet baseline levels, this easily applicable predictive score might be helpful to accurately select K-Ras WT mCRC patients who would benefit from P treatment. Further work is required to validate this approach in prospective cohorts of patients. Research Sponsor: None.