Development and Validation of a Prognostic Score for Overall Survival Integrating Baseline Metabolically Active Tumor Volume measured by $^{18}$F-FDG PET/CT and Clinical Factors for Metastatic Colorectal Cancer Patients

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Aim

This study aimed to develop and validate a prognostic score integrating baseline metabolically active tumor volume (MATV) and clinical factors in metastatic colorectal cancer (mCRC) patients.

Material and Methods

Material

- Development cohort: 160 unresectable chemorefractory mCRC patients enrolled in two prospective trials aiming to define an unlikely benefit from sorafenib/regorafenib (EudraCT numbers: 2010-023695-91 and 2012-005655-16).
- Validation cohort: 127 unresectable mCRC patients treated with chemotherapy and bevacizumab as first-line therapy enrolled in a prospective trial aiming to evaluate metabolic response parameters as predictors of outcome.
- 277 standardized baseline $[^{18}$F]fluorodeoxyglucose positron emission tomography-computed tomography ($^{18}$F-FDG PET/CT) scans were performed and analyzed.

Methods

- Target lesions delineation was performed using a PERCIST-based threshold.
- MATV was defined as the sum of metabolically active volumes of all target lesions.
- Baseline MATV biomarker has been demonstrated to have a high prognostic value both in the development and external validation cohorts, independently of patients’ treatment.
- A prognostic score for OS combining baseline MATV and clinical factors allowed to identify two risk groups of mCRC patients with significantly different mOS, in both the development and validation cohorts.
- MATV and the prognostic score for OS should provide a firm basis for risk stratification, in clinical practice and research trials.

Statistical analyses

- Optimal MATV cutoff for overall survival (OS) prediction was determined from the development cohort by the method of Williams.
- Multivariate analyses were done for OS including MATV and clinical variables (age, gender, BMI, ECOG PS, number of years between diagnosis and inclusion in the trial, presence of KRAS mutation).
- A prognostic score to predict OS was generated based on the parameters’ weights using Cox proportional hazards model.

Results

Fig 1: OS according to baseline MATV with a cutoff of 100 cm$^3$ in the development (A) and validation cohorts (B).

Fig 2: OS according to the prognostic score including baseline MATV and three clinical variables (ref. table 1) in the development (C) and validation cohorts (D).

Table 1: Prognostic score developed based on the combination of the independent predictors for OS retained in the multivariate analysis.

Conclusions

- Baseline MATV biomarker has been demonstrated to have a high prognostic value both in the development and external validation cohorts, independently of patients’ treatment.
- A prognostic score for OS combining baseline MATV and clinical factors allowed to identify two risk groups of mCRC patients with significantly different mOS, in both the development and validation cohorts.
- MATV and the prognostic score for OS should provide a firm basis for risk stratification, in clinical practice and research trials.

References


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