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Survival of patients with dMMR versus pMMR early stage colon cancer: A real-world matched study

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Background

Mismatch repair deficient (dMMR) colon cancer (CC) accounts for around 15% of non-metastatic CC pts. Although studies show that neoadjuvant immunotherapy may greatly improve outcomes, there are concerns of overstaging and overtreatment in a patient population presumed to have a good prognosis after surgery. In this study, we analyzed survival data of non-metastatic dMMR versus pMMR CC pts from the Netherlands Cancer Registry.

Methods

Pts with pathological stage 1-3 CC diagnosed between 2015-2019 who underwent resection without neoadjuvant treatment were identified from the registry. Only pts with available MMR status were included in the analysis, MMR deficiency was manually verified using pathology reports. Propensity score matching (max 1:4 ratio, 0.2 SD caliper) was used to balance age, sex, stage and ASA score. Differences were compared using Cox proportional hazard models. Follow up was restricted at 5 years.

Results

A total of 15456 pts were identified; 19% had verified dMMR tumors. Pts with dMMR CC were older, often female and had higher rates of poorly differentiated and mucinous tumors. In the matched cohort OS was similar between pts with dMMR ($n=2977$) and pMMR CC ($n=8949$) (HR 1.03; 95%CI: 0.96 – 1.12, $p=0.40$). When analyzed by pathologic stage, OS was similar between dMMR and pMMR pts with stage 2 ($n=1299$ vs 3445; HR 0.97; 95%CI: 0.82 – 1.15, $p=0.71$) and stage 3 ($n=1005$ vs 3442; HR 1.05; 95%CI 0.92 – 1.20, $p=0.50$; 5y OS 69% vs 68%) CC. 5 year OS rates of dMMR pts with pT1-3N+ ($n=732$), pT4N0 ($n=223$) and pT4N+ ($n=272$) were 77%, 71% and 49%, and for pMMR pts 75% ($n=2704$), 71% ($n=650$), 46% ($n=730$), respectively.

Baseline radiologic cT staging, often used to select pts for neoadjuvant therapy considering the inaccuracy of cN staging, was available for 2077 dMMR pts. Pts with dMMR cT4 tumors ($n=334$) had a 5 year OS of 64% regardless of pathologic staging.

Conclusions

This study, using real-world data from a registry cohort spanning 5 years, shows that MMR deficiency was not associated with an improved survival compared to pMMR CC, and 5 year OS rates in both pathological and clinical high risk stage 2 and stage 3 dMMR CC remain poor. Importantly, these data indicate that clinical staging can be used to select high risk pts for neoadjuvant immunotherapy.

Legal entity responsible for the study

Netherlands Cancer Institute.

Funding

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Disclosure

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