

Major response to immunotherapy in earlystage mismatch repair deficient colon cancer

October 22 2018

study design Microsatellite status dMMR: MMR deficient pMMR: MMR proficient pMMR **dMMR** (30)(30)This study Ipilimumab 1mg/kg Day 1 Ipilimumab 1mg/kg Day 1 Nivolumab 3mg/kg Day 1 + 15 Nivolumab 3mg/kg Day 1 + 15 + celecoxib 200mg daily Future amendments MUNICH ESVO

Credit: Annals of Oncology

Pre-operative treatment with a combination of the immune checkpoint inhibitors nivolumab and ipilimumab achieves major pathological responses in 100 percent of early-stage colon cancers with mismatch repair deficiencies, according to results reported at ESMO 2018 from the first exploratory phase II trial to investigate this approach.



Restoring patients' immune <u>response</u> against cancer cells with <u>checkpoint</u> inhibitors is an established <u>treatment</u> strategy for several tumour types. These agents are of particular interest in <u>mismatch repair</u> deficient (dMMR) tumours because they have high mutational load and upregulation of immune checkpoints.

Checkpoint inhibitors have previously shown durable responses in metastatic colorectal cancers so the new study investigated whether neoadjuvant treatment in dMMR early-stage colon cancer would achieve clinically significant response rates.

The exploratory trial treated 14 patients with early-stage colon cancer with the checkpoint inhibitors nivolumab (two doses of 3mg/kg on day 1 and 15) and ipilimumab (one dose of 1mg/kg on day 1) before surgery. The two drugs act in different ways to restore immune responses: ipilimumab blocks cytotoxic T lymphocyte associated protein 4 (CTLA-4) and nivolumab blocks programmed cell death protein 1 (PD-1).

Results reported at ESMO 2018 showed that 100 percent (7/7) of the patients with dMMR colon cancer had major pathological responses (defined as

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