Neoadjuvant immune checkpoint blockade in mismatch repair deficient endometrial cancer

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Background
Recent studies suggest neoadjuvant immune checkpoint blockade (ICB) may be more efficacious than adjuvant treatment in mismatch repair deficient (MMRd) cancers. However, this has not been explored for endometrial cancer (EC). Here, we report results from a phase I feasibility study of neoadjuvant pembrolizumab in 10 MMRd EC patients.

Methods
MMRd EC patients of any stage or grade at intent-to-treat with primary surgery (at least a hysterectomy) were eligible for participation, and 10/10 patients have been recruited. Patients were treated with 2 three-weekly cycles of pembrolizumab monotherapy (200mg iv) prior to standard-of-care resection and adjuvant treatment if indicated. Radiologic and pathologic response rates, treatment-related adverse events (trAEs) and immune correlates of treatment were assessed.

Results
Patients had stage I-II (n=4) or stage III (n=6) disease at diagnosis, remained on-protocol and underwent definitive surgery. In patients with measurable disease on MRI (n=8), a partial radiologic response was observed in 3/8 patients. A pathological response (<90% viable cancer cells) was observed in 5/10 patients, with 2 major pathologic responses (<10% viable cancer cells). To date, no recurrences have been observed, with a median and longest disease-free survival of 17 and 26 months, respectively. Subclonal MMRp was observed in 2 patients after neoadjuvant treatment. 9/10 patients experienced grade 1/2 trAEs. A treatment-induced immunological response was detected in 9/10 patients with increased lymphoid infiltrates, clonal T cell expansion and diverse T cell phenotypes in post-treatment samples. In tumour-draining (sentinel) lymph nodes, significant clonal overlap with treatment-induced intratumoural T cell expansion was demonstrated.

Conclusions
Neoadjuvant ICB is safe and feasible in MMRd EC. Two cycles of pembrolizumab induced pathologic, radiologic and immunologic responses. Investigation of extended neoadjuvant treatment is warranted and currently being evaluated.

Clinical trial identification

Legal entity responsible for the study
UMCG.

Funding
Dutch Cancer Society (drug supply by MSD without funding).

Disclosure

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