PEMBROLIZUMAB IN ADVANCED, RECURRENT CERVICAL CANCER – A CASE SERIES

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Introduction

- While the incidence and mortality of cervical cancer have decreased globally, prognosis still remains poor and treatment options are limited for the group of patients who develop recurrent or progressive disease after chemotherapy, radiotherapy and bevacizumab – best supportive palliative care is generally recommended at this stage.
- Immunotherapies, especially check-point inhibitors, have recently shown promising results in treatment of advanced solid tumours (1).
- Pembrolizumab is a programmed cell death 1 (PD-1) inhibitor, which has been approved by the US Food and Drug Administration for use in advanced melanoma, refractory Hodgkin lymphoma and non-small cell lung cancer (2).
- Binding of PD-1, normally expressed on T cells, to its ligand (PD-L1) results in T-Cell apoptosis and immune suppression through downregulation of T-cell receptor signalling(1).
- Recent studies indicate promising results for the use of Pembrolizumab in advanced, recurrent or persistent cervical cancer (3-5).

Aims & Objectives

- The aim of this study was to investigate the use of Pembrolizumab in heavily pre-treated patients with recurrent cervical cancer

Methods

- All consecutive patients with recurrent cervical cancer that had been treated with Pembrolizumab within clinical routine at the Comprehensive Cancer Center at the Medical University of Vienna, Austria, were included.
- Patients were considered for Pembrolizumab therapy through discussion at a multi-disciplinary tumour board, after they had received all other established treatment options.
- Pembrolizumab was administered at a fixed dose of 200mg intravenously every 3 weeks.
- Immunohistochemical analyses were performed to ascertain PD-1 status and mismatch repair (MMR) deficiency on tumour samples.
- A baseline CT scan was performed prior to Pembrolizumab initiation, and primary target lesions were identified and measured. CT scans were performed approximately every 3 months, and treatment response was evaluated according to the iRECIST (2017) criteria(6).
- Treatment was continued until disease progression or dose-limiting toxicity. In patients showing disease control or in selected patients with clinical benefit, treatment was continued even if iRECIST criteria indicated progressive disease.

Results

Patient characteristics

- 11 heavily pre-treated patients with current cervical cancer were included, with average age of 49 (range 26-65 years old).
- All had undergone previous chemo-radiotherapy containing cisplatin. 6 had previously received bevacizumab.
- 8 had squamous cell carcinoma, 2 adenocarcinoma, and 1 adenosquamous carcinoma.

Treatment toxicity

- Median number of Pembrolizumab cycles was 8 (range 1-17) and treatment was generally well tolerated.
- One patient discontinued therapy due to exacerbation of pre-existing ulcerative colitis; one patient had mild panniculitis on both forearms; one patient developed mild fever.

Overall response

Table 1: Best overall response	n	%
Clinical benefit rate (PR + SD)	4	36
Partial response (PR)	2	18
Stable disease (SD)	2	18
Progressive disease	7	64

- Figure 1 shows best change in tumour size from baseline.
- Figure 2 shows longitudinal change from baseline in tumour size.
- Median follow-up time was 27 weeks (range 3-53).
- Median time to progression was 8 weeks (range 3-9).
- Medial overall survival was 26 weeks (range 3-54).
- 6-month overall survival rate was 65%.
- 5 patients were PD-1 positive (PD-L1 expression >1%) and no patients showed micro-satellite instability.

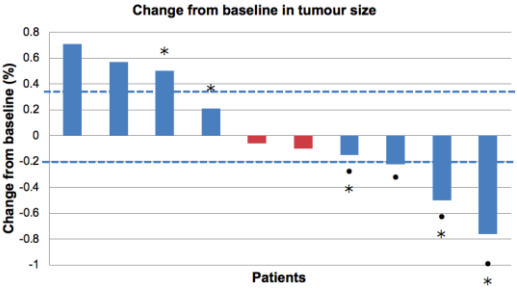

Figure 1: Change from baseline in tumour size (n=10). Dotted lines at 20% and -30% indicate the percentage change from baseline and represent progressive disease and response, respectively, as per iRECIST (2017). Dots indicate partial response and stable disease (clinical benefit). Stars indicate PD-L1 expression >1%.

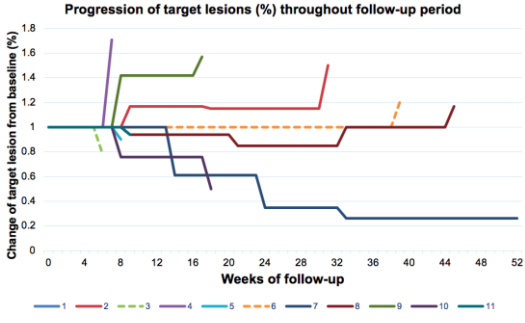

Figure 2: Longitudinal change from baseline in tumour size (n = 10). Two patients had no identifiable target lesions to follow, so progression of secondary lesions is represented, These patients are denoted with dotted lines. Target lesions are marked in denoted with continuous, non-dotted lines.

Conclusions

- Clinical benefit from treatment with Pembrolizumab was observed in one third of patients, and treatment was generally well tolerated.
- In patients responding to treatment, we observed durable anti-tumour activity of Pembrolizumab.
- PD-L1 over-expression was observed in all but 1 patient (who did not have sufficient tumour tissue for analysis) who had clinical benefit from treatment. None of the patients who did not respond had PD-L1 over-expression.
- Our results were comparable with the existing, limited, literature, which reported overall response rates of 17%.

References

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