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Potential impact of pembrolizumab in the adjuvant setting for intermediate-high risk and high risk kidney cancer

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Dear Editor,

Kidney cancer is one of the 10 most common cancers worldwide, with over 400,000 new cases diagnosed annually. In Ireland 650 new cases are diagnosed yearly[1].

High-risk kidney cancers refer to a subset of kidney cancers that are more aggressive and have a poorer prognosis compared to lower-risk variants.
Key characteristics of high-risk kidney cancers include:

- Larger tumor size (often >7 cm in diameter).
- Higher tumor grade (ISUP grade 3 or 4).
- Presence of adverse pathological features (e.g. sarcomatoid or N1 disease).
- Higher likelihood of metastatic spread at diagnosis M1 NED.

Partial or radical nephrectomy is the standard-of-care treatment for locoregional clear-cell renal-cell carcinoma. Surgery also has a role in the treatment of a highly selected group of patients with advanced renal cell carcinoma (M1 stage, indicating metastasis in a distant organ or tissue) with surgically resectable oligometastatic sites [2,3].

5-year overall survival rates for high-risk kidney cancer can be as low as 20%, compared to greater than 90% for low-risk disease. Patients diagnosed with renal-cell carcinoma who undergo nephrectomy lack effective adjuvant therapy options supported by substantial evidence [4].

We analysed our data of all the nephrectomies from January 2019 to January 2024, then compared our outcomes to the Keynote 564 trial results[3]. In their study, they found 151 (32%) of the patients developed recurrence and/or passed away without adjuvant pembrolizumab and a 32% reduced recurrence or death with pembrolizumab as adjuvant treatment compared to placebo (109 events of disease recurrence or death had occurred in the pembrolizumab group). Our primary end point was disease-free survival. Overall survival was a secondary end point.

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A total of 160 patients were followed at the prespecified interim analysis. 49 patients were matching the Keynote 564 trial inclusion criteria, but only 45 were included as they had local follow up. The median follow up was 15 months (range 2-58).

13 patients (28.9%) had metastasis and 32 (71.1%) were free of metastasis during the follow up period. 10 (76.9%) of those with metastasis had salvage treatment, while none of the included patients had adjuvant treatment. In those who had metastasis, 2 (15.3%) passed away – both had received salvage treatment. There was 1 (2.9%) death in those without metastasis. In total, 14 (31.1%) people went on to develop disease recurrence and/or pass away. The median time to developing a metastasis was 12.5 months from surgery (range of 2-38). The overall survival was 93% (42/45).

In conclusion, considering almost third of the patients had recurrence or death during their follow up and given the fact that the risk of disease recurrence or death was 32% lower with adjuvant pembrolizumab therapy than with placebo in the keynote 564 trial; the introduction of pembrolizumab as an adjuvant treatment within the Irish Healthcare Framework could have a significant impact in improving disease specific and overall survival.

Declarations of Conflicts of Interest:
None declared.

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