Immediate aggressive treatment may not be necessary for all adults with advanced kidney cancer

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Watch-and-wait approach means some patients could delay taking highly toxic non-curative anticancer drugs that come with substantial side effects

Some adults with advanced kidney cancer (renal-cell carcinoma) who have slow-growing disease can live for months and even years without the disease getting worse with active surveillance, or close monitoring for evidence of disease progression, instead of having to undergo immediate treatment with highly toxic anticancer drugs, suggests new research published in The *Lancet Oncology*.

The watch-and-wait approach was most successful in adults with limited sites of metastatic disease and those with one or less unfavourable prognostic factors such as anaemia, thrombocytosis (high platelet levels), and greater disability. For example, the 29 patients who had two or less organs affected and one or no risk factors at the start of the study remained on average almost three times longer on active surveillance than the other patients (22.2 months vs 8.4 months).

"There is a perception that all cancers should be treated immediately because they are equally lethal. But what we've seen in this small phase 2 study is that a subset of adults with advanced kidney cancer have slow-growing disease that can be safely managed using active surveillance, which could spare them the inconvenience and debilitating side effects

of aggressive treatments for about a year, and in some cases several years, without worsening anxiety and depression", explains lead author Professor Brian Rini from Cleveland Clinic Taussig Cancer Institute, Cleveland, Ohio, USA. "With just 50 people involved in our trial, the risk and benefits of the approach will need to be studied in a larger group of patients."

Every year, around 62700 new cases of kidney cancer are diagnosed in the USA and about 14240 people die from the disease; in the UK there are an estimated 11873 new cases and 4421 deaths from the disease. Survival varies widely from as short as 5 months in poor-prognosis patients without systemic treatment, to 43 months in patients with a good-prognosis who have systemic therapy.

When kidney cancer has spread to other parts of the body, the goal of systemic treatment is to slow the cancer down with antiangiogenic drugs like sunitinib and sorafenib that are designed to prevent the formation of new blood vessels, thereby stopping or slowing the growth or spread of tumours. But these treatments are expensive, not curative, and have serious side effects including increasing the risk of stroke and heart attack.

Some people with advanced kidney cancer have very slow-growing disease, and small case studies suggest that active monitoring and delayed treatment could be a safe, effective alternative to immediate systemic treatment, without compromising response to subsequent therapy.

In this phase 2 study, Rini and colleagues enrolled 52 adults (aged 18 or older) with advanced kidney cancer who had not received any previous systemic therapy from five hospitals in the USA, Spain, and the UK. Participants had a CT scan of the chest, abdomen, and pelvis at the start of the study and then at regular intervals to assess tumour burden and

time to disease progression. Patients were closely monitored and could decide with their physician to start systemic treatment at any time. Changes in quality of life, anxiety, and depression were also measured at the start of the study and over the surveillance period. Participants were followed for an average (median) of 38.1 months.

In the 48 participants included in the analyses, the average (median) time on active surveillance before starting systemic treatments was 14.9 months, and overall survival from the start of surveillance was 44.5 months.

43 (90%) participants experienced disease progression at some point during the study, most of whom (37) started systemic therapy. However, nearly half (20) of participants chose to continue on surveillance for an average of 15.8 additional months after disease progression. Six patients remain on active surveillance to this day. Three participants survived without the disease getting worse and two withdrew or were lost to follow up (figure 2).

Around half (22) of patients died during the study, but only one patient died (from brain metastasis) without ever receiving systemic therapy.

Importantly, quality of life, and anxiety and depression scores did not change substantially over the surveillance period (table 2), suggesting that living with untreated cancer did not cause psychological harm to patients with advanced kidney cancer in this study.

The authors sound a note of caution about the limitations of this trial which could reduce the broad applicability of the approach. For example, the patients included in the trial were a highly select group chosen by the treating physician rather than on the basis of disease characteristics such as tumour burden or pace of disease growth. Also, the decision to end surveillance was left to the discretion of the patient

and their physician.

According to Professor Rini, "With the development of novel immunotherapy in renal-cell carcinoma more work is needed to understand the risk and benefits of this initial observational approach. However, our data provides guidance about how to select patients who could delay treatment and instead be monitored safely with active surveillance."

Writing in a linked Comment, Dr Paul Russo from the Memorial Sloan Cancer Center, Weill Cornell College of Medicine, New York, USA says, "This paper provides guidance to both medical and surgical oncologists who, when faced with a newly diagnosed patient with metastatic renal-cell carcinoma who has good performance status and limited metastatic disease, can offer a period of close surveillance with the potential for prolonged survival before disease progression and the initiation of systemic therapies. There is no evidence from this study that such a period of close surveillance jeopardises the patient's safety or survival. It remains to be seen whether current genomic research can identify genes that can be used in conjunction with the above described selection factors to better choose patients suitable for initial active surveillance."

More information: *Lancet Oncology*, www.thelancet.com/journals/lan … (16)30196-6/abstract

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