

New research in kidney cancer, ASCO-GU 2017

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Checkpoint inhibitors

One of the key studies in kidney cancer presented at the American Society of Clinical Oncology 2017 Genitourinary Cancers Symposium (ASCO-GU) was the IMmotion150 study, comparing atezolizumab with or without bevacizumab to sunitinib among 305 patients with treatment-naïve, locally advanced or metastatic renal cell carcinoma (RCC).¹ Co-primary endpoints were progression-free survival (PFS) in the entire intention-to-treat cohort and PFS among patients with PD-L1 expression on $\geq 1\%$ of immune cells.

As shown in Fig. 1, there were no significant differences when comparing atezolizumab alone or the combination of atezolizumab plus bevacizumab with sunitinib. The median PFS was 6.1 months, 8.4 months, and 11.7 months for the atezolizumab alone, sunitinib, and atezolizumab plus bevacizumab arms, respectively. In the PD-L1-positive subgroup of patients, there was still no significant difference between the groups, although a trend in favour of the atezolizumab plus bevacizumab combination was noted (median PFS of 5.5 months, 7.8 months, and 14.7 months for the atezolizumab alone, sunitinib, and atezolizumab plus bevacizumab arms, respectively). Both experimental arms were well-tolerated, with no new or concerning safety signals. These results demonstrate that single agent atezolizumab has activity, but also support and show promise for the current phase 3 study (IMmotion 151; NCT02420821) comparing atezolizumab plus bevacizumab to sunitinib.

Also of interest was a retrospective analysis of data from the phase 3 CHECKMATE-025 study (nivolumab vs. everolimus in patients with metastatic RCC that failed one or two lines of systemic therapy).² The authors of this analysis sought to determine if treatment duration (time to treatment discontinuation [TTD]) for an immunotherapy is different from RECIST-defined PFS, which might explain the apparent lack of correlation between RECIST progression and overall survival (OS) observed in CHECKMATE-025. They reported that while there was no difference between TTD and PFS duration with everolimus in this study, the TTD was sig-

nificantly longer than PFS for nivolumab. They concluded that RECIST-defined PFS may not be appropriate for trials involving immune checkpoint inhibitors.

Targeted therapy

The impact of dosing strategies with sunitinib in RCC was also discussed. Canadian investigators, using data drawn from the Canadian Kidney Cancer information system (CKCis), presented an analysis comparing outcomes of patients in three groups: 1) those treated with sunitinib as per product monograph (SS; n=151); 2) those treated with sunitinib undergoing individualized dose/schedule changes (SI; n=355); and 3) those treated with pazopanib as per product monograph (PS; n=92).³ The key finding, as shown in Fig. 2, was that individualized treatment with sunitinib was associated with significantly longer OS compared to the other groups (median OS for SI, SS, and PS was 37.9, 22.3, and 19.6 months, respectively). Although confounded by small numbers in the pazopanib arm, these data only further support the growing body of evidence endorsing an individualized approach to managing metastatic RCC patients treated with sunitinib.

Predictors of long-term response in patients treated with pazopanib for advanced RCC was presented by Park et al, and in this study the authors performed a retrospective analysis of the U.S. Oncology Network's iKnowMed (iKM) electronic health record database.⁴ They examined the long-term responders to pazopanib, defined as patients with PFS >18 months on first-line pazopanib treatment. Of 153 patients treated with pazopanib, 21.6 % were identified as long-term responders, with PFS 27.2 months, Eastern Cooperative Oncology Group performance status (ECOG PS) score of 0, and a history of nephrectomy — significant predictors of long-term response.

Active surveillance before systemic therapy in metastatic RCC

In the last years, a number of retrospective studies reported outcomes of patients on active surveillance (AS) for metastatic

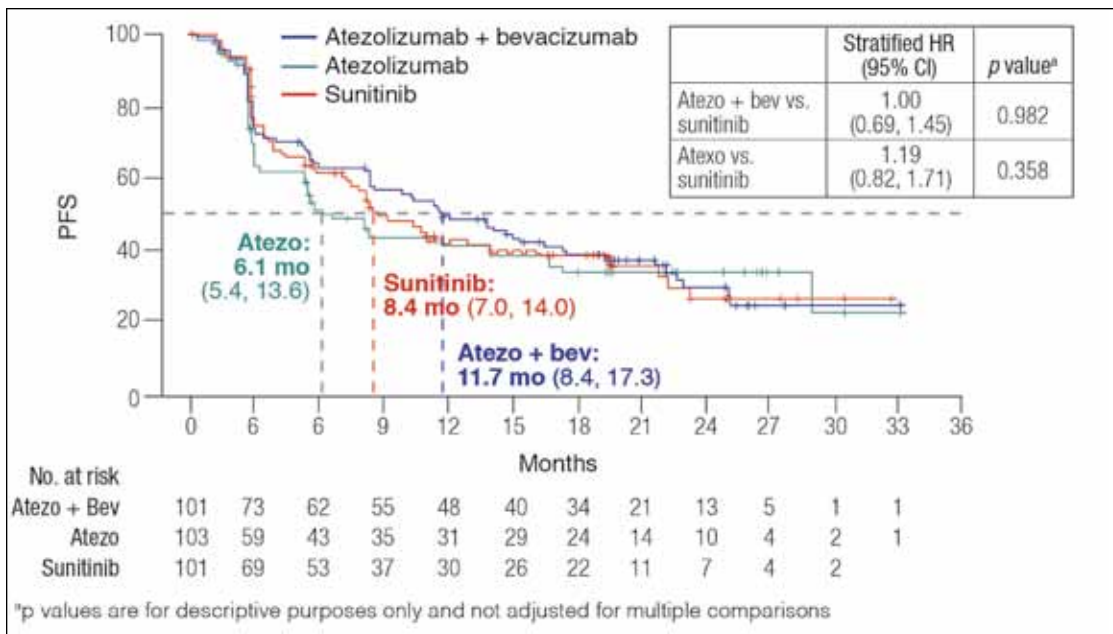


Fig. 1. Progression-free survival in the IMmotion150 trial: Atezolizumab ± bevacizumab vs. sunitinib. CI: confidence interval; HR: hazard ratio.

RCC. In a prospective series, Italian investigators presented their data of an AS cohort of 52 metastatic RCC patients in a single centre.⁵ Outcomes included time on surveillance, PFS, OS, and post-surveillance OS. A key finding was that only four patients on AS had a worsening of their prognostic grouping (i.e., good to intermediate) as per International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria

at a median time on AS of 19.9 months. It was also noted that increase in tumour burden and number of metastatic sites was related to a worse post-surveillance survival. Overall, while AS may be a reasonable option for some IDMC good- and intermediate-risk patients selected by experienced physicians, more studies are needed to more objectively determine for which patients this would be appropriate.

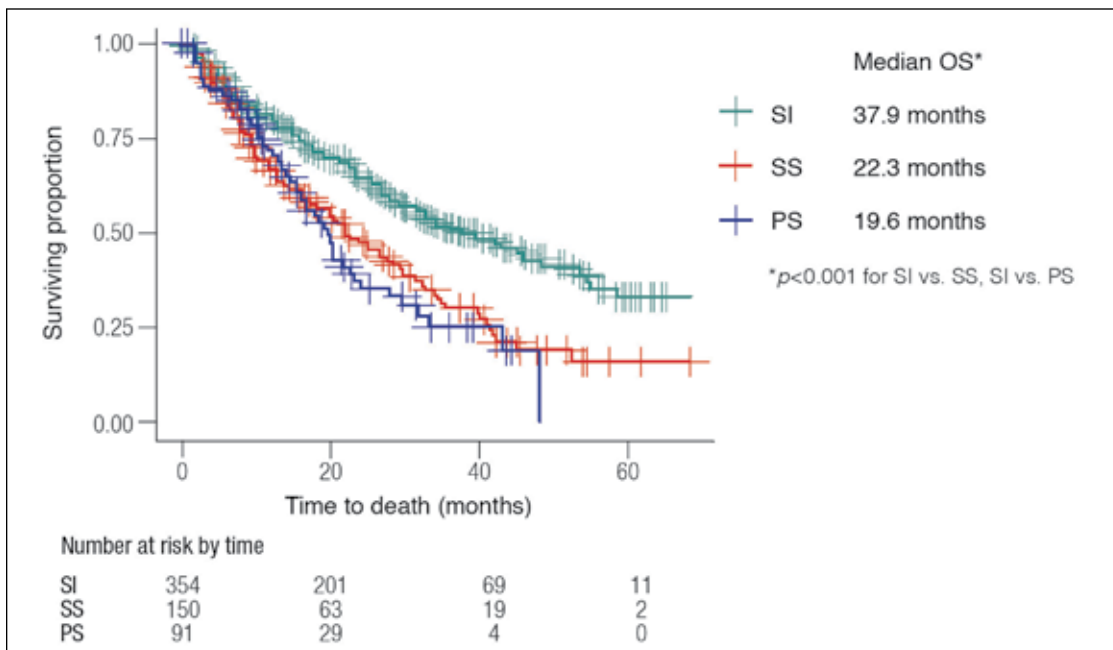


Fig. 2. Overall survival (OS) by dosing strategy for vascular endothelial growth factor (VEGF) inhibition in the Canadian Kidney Cancer Information System (CKCis). SI: sunitinib with individualized dose/schedule changes SS: sunitinib as per product monograph; PS: pazopanib as per product monograph.

Active surveillance for small renal masses

A separate analysis from the U.S. Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) registry evaluated the efficacy of AS compared to primary intervention among 615 patients with small renal masses (≤ 4.0 cm, clinical stage T1a) who chose to undergo primary intervention (e.g., surgery, ablation) or AS.⁶ After a median followup period of three years, the five-year cancer-specific survival (CSS) rates were found to be comparable for the two groups (100% vs. 99.8%; $p=0.3$); however, 45.6% of patients had crossed over to treatment at five years. Moreover, OS was markedly lower in the AS group (an observation the authors attributed to the older age and worse overall health of this group). These midterm results show that AS for pT1a renal mass is a safe approach for patients with limited life expectancy; however, long-term median followup will be needed to extrapolate these results to patients with >5 -year life expectancy.

Surgery

Several presentations at ASCO-GU 2017 provided important new information with respect to surgical approaches to RCC. Investigation of the U.S. National Cancer Database from 2006–2013 showed that the predominant therapeutic approach was systemic therapy alone (53%).⁷ Twenty-two percent received cytoreductive nephrectomy (CN) alone and a further 22% had CN and then systemic therapy. Only 3% had systemic therapy followed by CN. Median time to systemic therapy after CN was 45 days, but 73% of patients received it within 30 days. CN was, however, associated with a 90-day mortality risk of 10%, for which

high tumour burden, older age, and comorbidities were risk factors. These results show that most patients will be able to receive short-term systemic therapy after CN, but patient and tumour factors must be taken into consideration when selecting candidates.

A separate analysis of the same database showed that, among patients who received CN after systemic therapy, OS was significantly longer than among those who only received systemic therapy (median OS 19.0 vs. 4.9 months).⁸ These results, despite being biased by patients and tumour factors, support those already published in 2014 by Heng et al.⁹

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