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Short Communication

The Best of the Genitourinary Cancers Symposium 2021 in Kidney Cancer

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The congress of the American Society of Oncology on genitourinary tumors, held virtually between February 11 and 13, 2021, is one of the largest congresses on genitourinary neoplasms. Next, we will review the works that have attracted the most attention in kidney cancer.

Treatment in patients with metastatic renal cell carcinoma (mCRC) has changed dramatically in recent years. The era of immunotherapy began with the CheckMate214 study, the combination of nivolumab and ipilimumab (NIVO + IPI) compared with sunitinib (SUN) demonstrated a benefit in survival and increased responses to treatment. However, data on recurrence and disease progression patterns with immuno-oncological agents are still scarce [1].

In this congress, the results of the evaluation by progression patterns with NIVO + IPI vs. SUN. After a minimum follow-up of 4 years, the progression patterns were defined by a growth of ≥ 20% of the target lesion, unequivocal progression of the non-target lesions, and the appearance of new lesion (s) (LN). Response and progression were assessed by an independent radiological review committee using RECIST v1.1 [1].

Radiological progression was documented in 299/550 (54.4%) patients with NIVO + IPI versus 289/546 (52.9%) with SUN. The pattern of radiological progression differed between the arms: with NIVO + IPI, 106/299 (35.5%) resulted only in NL versus 74/289 (25.6%) with SUN, and this difference was more pronounced in patients with an initial response confirmed (36/71 [50.7%] vs. 23/84 [27.4%]) [1].

Most of the radiological progressions of only LN in the initial responders occurred in a single organ (34/36 [94.4%] for NIVO + IPI; 20/23 [87.0%] for SUN, the most frequent sites being the lymph nodes (11/34 [32.4%]), brain (8/34 [23.5%]) and lung (5/34 [14.7%]) with NIVO + IPI, and lymph nodes (7/20 [35.0%]), brain (4/20 [20.0%]) and adrenal gland (3/20 [15.0%]) with SUN [1].

This analysis allowed us to observe the differential radiological patterns of tumor relapse and disease progression after long-term follow-up; resulting in that the progression of LN occurred more frequently with NIVO + IPI versus SUN and in a particular way in the subgroup of patients who progressed after having obtained a response with the treatment, reaching these radiological patterns have therapeutic implication [1].

The JAVELIN Renal 101 trial demonstrated the superiority of avelumab + axitinib (AVE + AXI) compared to sunitinib (SUN) in patients with mCRC; however, the role of the combination of immunotherapy + VEGFR inhibition in elderly patients is still unclear. At this conference, Dr. Yoshihiko Tomita and his colleagues provide an update of age-stratified efficacy and safety results [2].

Age stratification was as follows: 271, 138, and 33 patients aged < 65, ≥ 65 to < 75 and ≥ 75 years, respectively, were randomized to receive avelumab + axitinib; while 275, 128 and 41 patients were randomized to receive sunitinib [2].

The proportion of risk groups according to the International Consortium of mCRC databases (IMDC) was equitable in each age group of both arms; however, in the subgroup aged ≥ 75 years, the frequency of intermediate-risk patients was slightly higher in the CVA + AXI group, and that of favorable-risk patients was slightly higher in the SUN group. The median follow-up was 19 months in the CVA + AXI group and 16 months in the SUN group. The benefit of the combination was constant in the age groups; especially in terms of objective response rate (ORR) and progression-free survival (PFS). The most common treatment-related adverse events were diarrhea, hypertension, palmar-plantar erythrodysesthesia syndrome, fatigue, and nausea [2].

The combination AVE + AXI shows favorable efficacy in all age groups, including patients older than 75 years [2].

KEYNOTE-426 is a phase III, randomized, open-label trial studying the combination treatment of pembrolizumab + axitinib (PEMBRO + AXI) that has been shown to significantly improve OS, PFS and ORT compared to sunitinib (SUN) as a first-line treatment. line for patients with mCRC [3].

During this congress, Dr. Plimack and collaborators provide us with an update on this study focused on the group of patients who received PEMBRO + AXI and who completed two years of follow-up [3].

Of 432 patients treated with PEMBRO + AXI, 129 (29.9%) completed 2 years of treatment. 72.1% were men with a median age of 61 years (36 - 82); 42 (32.6%) and 87 (67.4%) patients had favorable and intermediate/low risk according to the IMDC, respectively. The median follow-up was 31.1 (24.0 - 37.7) months [3].

For patients who completed the two years of treatment, the OS rates at 36 months were 93.8% (95% CI, 85.5% - 97.4%). The PFS at 24 and 36 months were 72.7% (95% CI, 64.0% - 79.7%) and 57.7% (95% CI, 46.3% -67.5%), respectively. The ORR was 85.3% and the complete response rate was 14.0%. 59.7% of patients experienced grade 3 - 5 treatment-related adverse events and 8.5% experienced grade 3 - 5 immune-mediated adverse events [3].

This analysis allows us to conclude that the proportion of patients who completed 2 years of treatment with combination therapy maintain a clinical benefit with a safe toxicity profile [3].

New analyzes of the Phase III CheckMate 9ER trial, an open-label, randomized 1: 1 study of nivolumab + cabozantinib (NIVO + CABOZ) vs. sunitinib (SUN) were presented at this congress. At a median follow-up of 23.5 months, sustained and significant efficacy has been demonstrated in relation to PFS, ORT and OS in favor of the combination for the first-line treatment of patients with mCRC [4].

In the total population, the combination doubled the PFS (17 months vs. 8.3 months; HR: 0.52; 95% CI, 0.43 - 0.64). In addition, it showed a 34% reduction in the risk of death compared to sunitinib (HR: 0.66; 95% CI, 0.5 - 0.87). The disease control rate (complete response, partial response, and stable disease) was 88.2% vs. 68.9%, respectively. The complete response rate for the combination was 9.3% vs. 4.3% with SUN. Regarding adverse effects, of the patients receiving the combination, only 6.6% interrupted doses (9.7% only NIVO and 7.2% only CABOZ) [4].

In the subgroup analysis, of 75 (11.5%) patients with sarcomatoid histology, 34 were randomized to receive combination therapy vs. 41 patients received SUN. After a median follow-up of 18.1 months, the combination was shown to reduce the risk of death by 64% compared to SUN (HR: 0.36; 95% CI, 0.17 - 0.79), a higher PFS of 10.3 months vs. 4.2 months and an objective response rate of 55.9% versus 22% [4].

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