Universitätsmedizin Essen

Final results on efficacy and patient reported outcomes (PRO) of a randomized phase II trial investigating nivolumab switch-maintenance after TKI induction in metastatic clear cell renal cell carcinoma (mRCC) patients (NIVOSWITCH)

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Background

In mRCC combinations of tyrosine kinase inhibitors (TKI) and checkpoint inhibitors (CPI) are considered standards of care

Primary objective:
- To assess the survival benefit from an early switch-maintenance approach (CPI after TKI) in mRCC.

Secondary objective:
- Investigating whether a 1st line switch-maintenance approach (CPI after TKI) improved outcome in mRCC.
- Impact of switch-maintenance approach on PROs and thus quality of life over time

Methods

Participants
- mRCC patients with partial remission (PR) or stable disease (SD), with ECOG 0-2 and adequate organ function
- First-line treatment with a TKI for 10-12 weeks

Assesments
- Patient-reported outcomes (PRO) were assessed by the FACT Kidney Symptom Index (FKSI-15)
- The trial was recruiting patients between 2016 and was prematurely closed on August 2018 due to low accrual rate
- Data base was closed on December 2020

Results

- Response to TKI induction therapy was PR in 59% and SD in 41% of patients
- ORR from randomization favored TKI continuation with 16 vs. 48% (p=0.03)
- PFS was 3.0 vs. 11.9 mo. (HR = 2.57 [95% CI: 1.36 – 4.89]) in favor for TKI continuation.
- Mean FKSI-15 score at therapy initiation to end of therapy showed no significant difference
- Median TTD favoured NIVO (NR) vs. TKI (6.9 mo), but difference remained insignificant (P=0.16)
- Median OS was not reached. 2-year OS was 64% for NIVO and 66% for TKI treatment (HR = 1.12 [95% CI: 0.43 – 2.89]; P=0.82)

Conclusion

- Maintenance-switch with nivolumab did not improve efficacy vs. continuation of TKI therapy
- Continuation of TKI therapy achieved a higher response rate (52% vs. 20%) and significantly higher PFS vs. Nivolumab switch-maintenance therapy (HR 2.57; p=0.003)
- Although a lower degree of grade ≥3 AEs for NIVO was observed (56% vs. 71%), a PRO benefit was not detected

Limitations:
- Early discontinuation of the study
- Small sample size
- Selection of TKI-sensitive patients

Parameter		Nivolumab n=25	TKI n=24
Age	Mean ± SD	63.9 ± 9.5	66.4 ± 8.5
	Median (Range)	65 (35-78)	66 (48-79)
Gender	Female	4 (16%)	5 (21%)
	Male	21 (84%)	19 (79%)
MSKCC overall risk assessment	Favorable risk group	8 (32%)	7 (29%)
	Intermediate risk group	16 (64%)	16 (67%)
	High risk group	1 (4%)	1 (4%)
Duration of therapy	Median (Range)	3.9 (2.5-8.3)	9.7 (5.7-19)
Follow up	Median (Range)	26.3 (1.3-45.6)	26.2 (3-43.8)

Table 1: Table 1. Main patient characeteristics. Data are displayed for both groups and in total.

	Nivolumab n=25	TKI n=24
ORR	5 (20%)	12 (52%)
CR	0 (0%)	2 (9%)
PR	5 (20%)	10 (43%)
SD	6 (24%)	6 (26%)
PD	12 (48%)	3 (13%)
NE	2 (8%)	2 (9%)

Table 2. Main patient characeteristics. Data are displayed for both groups and in total.

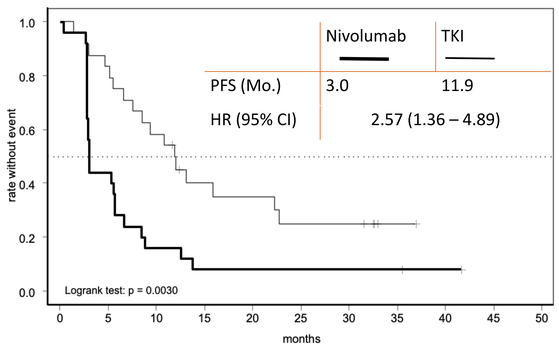

Figure 1. Progression-free-survival of Nivolumab and tyrosin kinase inhibitors (TKI).

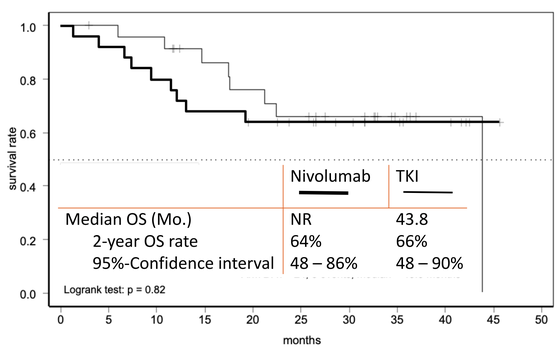

Figure 2. Overall survival (OS) of Nivolumab and tyrosin kinase inhibitors (TKI).

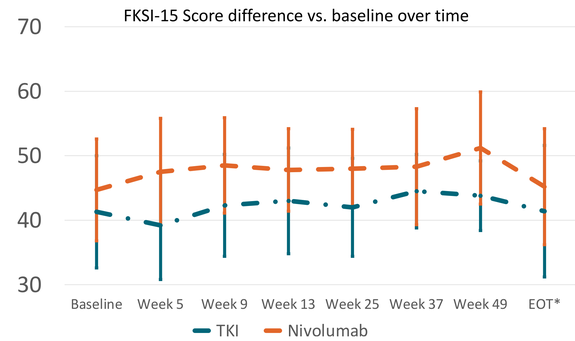

Figure 3. FACT Kidney Symptom Index (FKSI-15) of both groups. Data are given in mean ± standard deviation at several time points. EOT*: end of study treatment

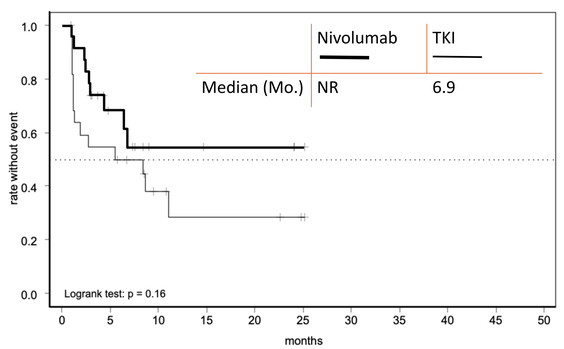

Figure 4. Kaplan-Meier estimate of the time to deterioration.

Parameter	Nivolumab n=25	TKI n=24
Average number of AEs per patient	10.6	13.2
Patients with at least one AE (all grades)	24 (96%)	24 (100%)
Patients with at least one AE of grade 3-5	14 (56%)	17 (71%)
Patients with SAE	12 (48%)	12 (50%)
Interruption/modification of schedule	0 (0%)	6 (25%)
Dose adjustment or discontinuation	4 (16%)	13 (54%)
Discontinuation due to toxicity	1 (4%)	4 (17%)

Table 2. Overview of adverse event reports.

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