Optimizing Ipilimumab in metastatic renal cell carcinoma
SAKK 07/17 study

e-Poster
#3404

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ABSTRACT

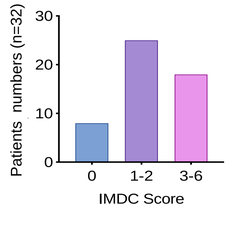
Nivolumab (Nivo) + Ipilimumab (Ipi) is an approved 1st line treatment for advanced RCC patients (pts) with an International Metastatic RCC Database Consortium (IMDC) intermediate or poor risk score. The CheckMate 214 (CM-214) study showed superior outcomes for Nivo + Ipi compared to Sunitinib in these pts. Whether the induction of CM-214 with 4 cycles of Ipi (1mg/kg/q3w) and Nivo (3mg/kg/q3w) followed by a maintenance treatment of Nivo (3mg/kg/q2w) is the optimal scheme regarding efficacy and safety remains to be determined. The SAKK 07/17 study aims to reduce toxicity (AEs) by individualizing Ipilimumab applications. Clinical trial identification: NCT03297593.

METHODS

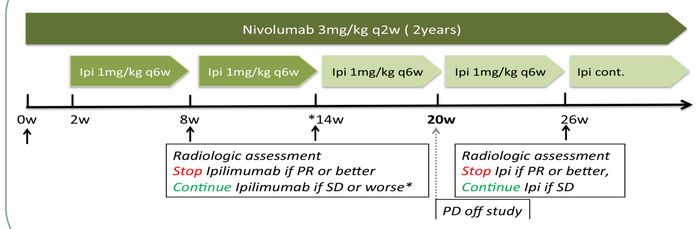
The SAKK 07/17 trial is an ongoing adaptive-design, prospective single-stage single-arm multicenter phase II trial in Switzerland with an enrolment goal of 74 participants. In the first cohort 32 patients with metastatic RCC (mRCC) and predominantly clear cell histology and any IMDC risk entered the study for 1st or 2nd line (post-TKI) treatment with Ipi and Nivo between 12/ 2017 and 02/2019. The treatment scheme for the 1st and 2nd cohort is as follows:
Pts. start treatment with Nivo (240mg q2w until wk20, 480 mg q4w thereafter). After 2 weeks Ipilimumab 1mg/kg/q6w was introduced. As soon as a radiographic complete response (CR) or partial response (PR) is observed, Ipi is stopped and Nivo is continued for a maximum of 2 years. The primary endpoint is the objective response rate (**ORR**) per RECIST with a rate of ≤ 20% regarded as unpromising and ≥ 40% as promising activity. Secondary endpoints include PFS, DOR, TTF, OS, AEs. For the translational research an integral part of this trial, biospies and blood were taken before. The clinical results of the FAS* of the first cohort with a median follow-up time of 18.3 mo and initial findings from the translational research (TR) part are reported.

*FAS: Full Analysis Set: All subjects who received at least one dose of both treatment drugs

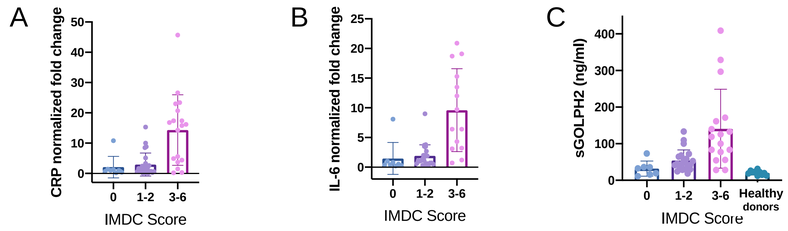
Pts. Baseline characteristics	Baseline characteristics (N=32)
	Median age, years 69
	Male, % 81.3
	IMDC risk score, %
	Good 12.5
	Intermediate 53
	Poor 34.5
	Location of metastasis, % (multiple, N=21)
	Lung 81
	Bone 42.9
	Brain 14.3
	Perinephrium 28.6
	other 61.9
	WHO performance status, %
	0 43.8
	1 56.2
	Previous therapy, % 21.9



Trial scheme

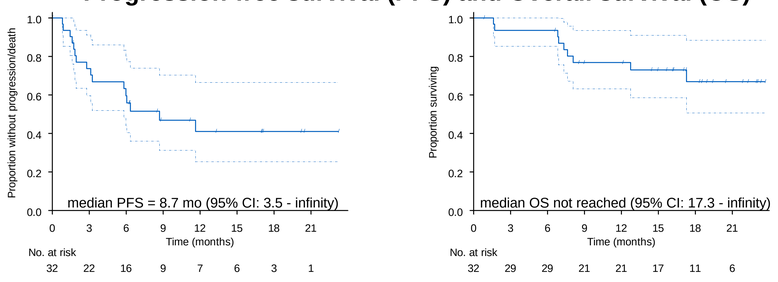


Association of IMDC Scores, CRP, IL-6 and sGOLPH2 at Baseline

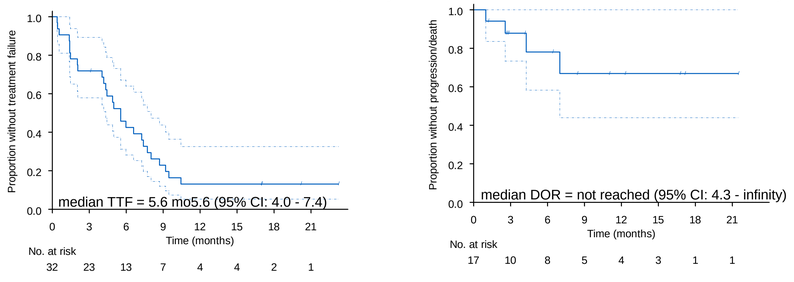


Correlation of IMDC Scores and Serum Markers
A-C selected serum markers at baseline. **A, B** CRP and IL-6 are depicted as fold change compared to the respective normal values of the participating centers.
C Pts. sGOLPH2 values shown in comparison to values of a healthy donor cohort.

Progression-free survival (PFS) and Overall survival (OS)



Time to treatment failure (TTF) and Duration of response (DOR)



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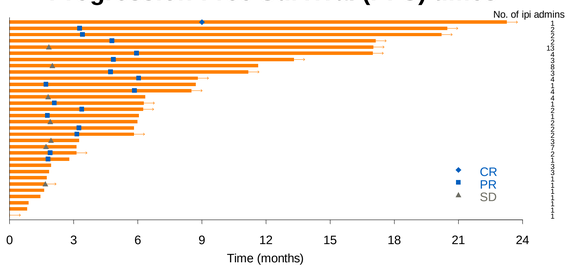
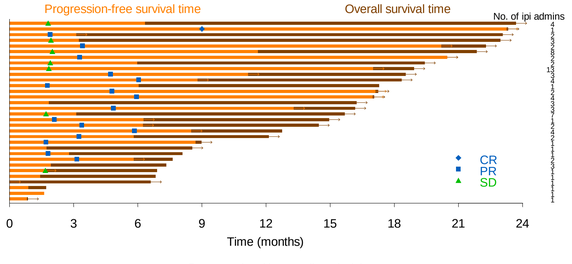
Progression-Free Survival (PFS) times



Pts. are ordered by progression-free survival times. 16/32 pts. continue treatment.

PFS and Overall Survival (OS) times



Pts. are ordered by overall survival times

RESULTS

Of the total of 32 pts, 25 pts were treated in 1st and 7 pts in 2nd line (post-TKI). Median age was 69 y (range 48-86). According to IMDC risk score 12.5% had favourable, 53% intermediate and 34.5% poor risk. At a median follow-up of 18.3 months (mo), the **ORR** was **53.1%** (CR=3.1%, PR=50%, SD=21.9%, PD=18.8 %, NA=6.3%) (ORR 90% CI 39% - 68%, p < 0.001 (one-sided)). The frequency of AEs and SAEs was comparable to established standards. Elevated levels of CRP, IL-6 and sGOLPH2 were factors associated with higher risks IMDC scores at baseline.

DISCUSSION

The analysis of the first cohort of this prospective I/O trial in mRCC shows an alternative Nivo/Ipi regimen to be safe, feasible and efficacious. The longer intervals of Ipi (q6w) and the option to reduce or to increase the doses of Ipi (median dose of Ipi = 1.0 mg/kg) have not negatively affected the outcome. ORR, PFS and OS are in the range of the CM-214 (1,2), despite 22% of pts. been treated in second line. The lower rate of CRs in this study is likely to be attributable to the current case number and ought not be overinterpreted. The prognostic markers and their potential predictive value will be further evaluated in the combined analysis of the 2 cohorts.

CONCLUSIONS

SAKK 07/17 is the first adaptive design study to assess the impact of a reduced dose, prolonged Ipi administration guided by response in the combination treatment of mRCC. Regarding ORR the strategy is promising and does not appear to be inferior to CM-214. The TR data suggest an association of CRP, IL-6 and sGOLPH2 and prognosis. These findings support further exploration and possibly integration of the new serum markers for prognostication in pts. with RCC. Further analysis is ongoing to assess all endpoints including duration & depth of response.

Conflicts of interest: FS declares financial support and/or advisory boards: BMS, MSD, Roche, Ipsen, Merck.
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Note: [5]Dr. A Patrikidou's current affiliation: Sarah Cannon Research Institute and UCL Cancer Institute, London, UK

Literature
(1) CM-214 (N Engl J Med 2018; 378:1277-1290 Motzer RJ et al.)
(2) Updated CM-214 (Tannir NM et al. ASCO GU 2020)