Die SAKK auf dem ASCO-Jahrestreffen 2019

Die Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK) präsentierte auf dem diesjährigen Jahrestreffen der ASCO und zuvor im Februar auf dem Kongress ASCO-GU – teilweise in Zusammenarbeit mit ausländischen onkologischen Studiengruppen – mehrere klinische Studien in Poster Sessions und in Oral Sessions. Eine Auswahl ist hier in der englischen Originalversion mit den jeweiligen Ansprechpartnern zusammengestellt.

Metastatic colorectal cancer (mCRC)

Bevacizumab (BV) maintenance (M) after first-line chemotherapy (CT) plus BV for metastatic colorectal cancer (mCRC) patients (pts): a meta-analysis of individual pts data (IPD) from 3 phase III studies. (SAKK 41/06).

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From Switzerland: Prof. Dr. med. Dieter Köberle, Claraspital Basel
Abstract #261885.

Background
Although CAIRO3- and AIO KRK 0207-trials demonstrated the benefit of BV + fluoropyrimidine as a maintenance (M) regimen after induction CT + BV, the role of BV alone is not clear. Indeed, SAKK 41/06- and PRODIGE 9- trials failed to demonstrate the superiority of BV alone vs. no M, while AIO KRK 0207 showed the non-inferiority of BV alone vs. combination M.
Thus, in order to evaluate the magnitude of the eventual benefit of M with BV alone vs. no M, an IPD-meta-analysis was performed.

Methods
Trials whereas mCRC pts were prospectively randomized to receive BV-M or not were considered eligible. Primary endpoints were PFS and OS, both from the start of induction and M. Univariate and multivariate analyses for PFS and OS were performed, with the following variables: baseline ECOG-PS; age (> vs ≤ 65 years); RAS- and BRAF- status; LDH- and CEA-baseline level; RR (PR or CR vs. SD) during induction; induction-CT (oxa- vs. iri-based); resected primary tumor; primary tumor side; synchronous vs metachronous; adjuvant treatment; number (N) of metastatic sites; liver-only disease.

Results
IPD of 1,064 pts enrolled in the PRODIGE 9, AIO KRK 0207 and SAKK 41/06 -trials were collected. Considering the different timing of randomization in PRODIGE 9 (at the start of induction) vs. AIO KRK 0207 and SAKK 41/06 (at the start of M), IPD of pts not progressed during induction and starting M-phase entered the analysis. 909 pts were included, 457 (50%) received BV-M.
Median PFS from induction start was 9.6 and 8.9 months in BV-group vs. no M-group, respectively (HR 0.78; 95%CI: 0.68–0.89; $p < 0.0001$). At the multivariate PFS analysis, BV-M, resected primary tumor, number of metastatic sites and liver-only disease were significant. No difference in terms of OS between the 2 groups was observed.

Conclusions
This is the first IPD-meta-analysis investigating the role of BV alone M vs. no M after first-line induction CT+BV in mCRC pts. Despite the significant PFS improvement in favor of BV-M, the absolute benefit appears limited, and without a clear clinical relevance. On these bases, a predictive nomogram to identify pts most likely to benefit from BV-M is under evaluation and will be presented during the Congress.

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Genitourinary Cancer Symposium 2019 of the American Society of Clinical Oncology, San Francisco, 14. bis 16. Februar 2019

Die SAKK auf dem ASCO-GU 2019

Castration resistant prostate cancer

Incidence of hypocalcemia (HC) in patients with castration resistant prostate cancer treated with denosumab (DN): Data from a non-inferiority phase III trial assessing prevention of symptomatic skeletal events (SSE) with DN administered every 4 weeks (q4w) versus every 12 weeks (q12w): SAKK 96/12 (REDUSE)

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Abstract #GU19

Background
DN given q4w has shown superiority in delaying skeletal related events over q4w zoledronic acid (ZA). Recently it has been demonstrated that ZA q12w is non-inferior to ZA q4w. The objective of REDUSE is to show non-inferiority for DN q12w versus q4w in terms of SSE. Here we present an interim analysis for the secondary endpoint HC.

Methods
Patients (pts) with castration resistant prostate cancer (planned N=690) were randomized 1:1 to DN q4w (Arm A) vs q12w (Arm B) after a 16 week induction phase with application q4w. All pts received vitamin D (ViD) 400 U and calcium (Ca) 500 mg daily. Measurement of corrected serum-Ca was mandatory before each DN injection. This interim analysis was performed after 3.5 years of accrual. Men who received ≥ 1 dose of DN were considered evaluable.

Results
282 pts were evaluable. HC occurred in 28.7% during the first 16 weeks (DN q4w for all pts) and 30.2% afterwards. After the induction phase HC occurred in 40.2% in Arm A and in 20.3% in Arm B. Grade 3 (2.1%) and 4 (1.1%) HC were rare, most frequently occurring in the first 16 weeks. After 1 year of treatment, the incidence of HC was lower in both arms (A: 30.8%, B: 18.7%). A clinically relevant difference for HC was noted between the two arms after the induction phase (*table*).

Conclusions
In our trial nearly 30% of all men treated with DN experienced HC in the q4w induction phase despite mandatory supplementation of calcium and ViD and measurement of Ca. This rate was considerably higher than reported in the registration trials of DN (13%). After induction treatment the incidence of HC is considerably lower in the q12w arm compared to q4w. This suggests that DN given q12w has a more favorable long time toxicity profile (HC) compared to DN q4w.

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Table:
Change in HC grade after week 16 (week 1 – 12: DN q4w Arm A+B), thereafter q4w in Arm A and q12w in Arm B.

	Arm A (N = 57) n (%)	Arm B (N = 44) n (%)
Worsening of HC grade	23 (40.4%)	15 (34.1%)
HC grade unchanged	19 (33.3%)	6 (13.6%)
Improvement of HC grade	15 (26.3%)	23 (52.3%)