Die SAKK auf dem ASCO-Jahrestreffen 2015

Die Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK) präsentierte auf dem diesjährigen Jahrestreffen der ASCO – teilweise in Zusammenarbeit mit ausländischen onkologischen Studiengruppen – mehrere Abstracts klinischer Studien in Poster Sessions und in Oral Sessions. Wir stellen auf diesen Seiten die Abstracts (#) in der englischen Originalversion mit den jeweiligen Ansprechpartnern zusammen.

Non small cell lung cancer; squamous (SqNSCLC)

Studie: «Randomized phase III trial of erlotinib vs. docetaxel in patients with advanced squamous cell non-small cell lung cancer (SqNSCLC) failing first line platinum based doublet chemotherapy stratified by VeriStrat Good vs VeriStrat Poor: The European Thoracic Oncology Platform (ETOP) EMPHASIS trial.»

First Author: Solange Peters, University Hospital of Lausanne (CHUV), Lausanne
 # 8049 Poster Session (Board #372)

Background: Docetaxel (D) or Erlotinib (E) are registered second-line treatments for EGFR wild type NSCLC. Previous studies suggested a predictive value of the serum proteomic VeriStrat test (VS), assigning a good (VSG) or poor (VSP) classification in second-line therapy of patients (pts.) with NSCLC. EMPHASIS aimed at exploring a predictive interaction in SqNSCLC pts. The trial closed prematurely due to low accrual.

Methods: EMPHASIS is a randomized phase III multicenter trial exploring the differential activity of second line E vs. D on progression-free survival (PFS) in VSG vs. VSP SqNSCLC. The expected hazard ratio (HR) of E vs. D was 0.675 for the VSG patients (median PFS, E: 4.0 and D: 2.7 mo.), and 1.23 for the VSP patients (median PFS, E: 2.2 and D: 2.7 mo.). A sample size of 500 was needed to achieve 86% power for testing the expected interaction HR of 1.82 at a two-sided p-value of 0.05. Pts were randomized to receive treatment E150 mg p.o. daily or D 75 mg/m^2 i.v. on day 1 of each 21 day cycle.

Results: From 1/2013 to 1/2014, a total of 80 patients were randomized to the study, with 72.5% categorized as VSG. Median age was 69 years with the majority being male (83%), smokers (94%), and having good performance status (91%). No unexpected serious adverse events (SAEs) were observed in either treatment arm. All pts are off treatment (median time to treatment failure: 2.1 mo.), while 73 progression events (median PFS: 2.7 mo.) and 56 deaths (median OS: 7.1 mo.) were observed. Median PFS for VSG is 4.1 and 1.6 mo. under D and E respectively, and 1.9 and 2.1 mo. for VSP pts (HR = 1.04, interaction p-value = 0.94). Median OS for VSG is 7.8 and 8.4 mo. for D and E and 4.4 and 5.2 mo. for VSP.

Conclusions: The final analysis of EMPHASIS did not show a differential activity on PFS of E vs. D in SqNSCLC pts stratified by VS status. These results are at variance with trial assumptions and previous studies. In addition to the EMPHASIS results (PFS & OS), we will present a combined PFS/OS analysis with the subgroup of SqNSCLC from the PROSE study.
EudraCT number: 2012-001896-35.
Clinical trial information: NCT01652469.

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Soft Tissue Sarcomas (STS)

Studie: «GeDDiS: A prospective randomised controlled phase III trial of gemcitabine (Gem) and docetaxel (Doc) compared with doxorubicin as first-line treatment (Dox) in previously untreated advanced unresectable or metastatic soft tissue sarcomas (EudraCT 2009-014907-29).»

First Author: Beatrice M. Seddon, University College Hospital, New Malden, United Kingdom
 # 10500 Oral Abstract Session

Background: Standard first-line treatment of locally advanced/metastatic soft tissue sarcoma (STS) is Docetaxel (Dox). GemDoc (Gemcitabine/Docetaxel) has activity in STS and is used in relapsed STS after failure of at least one line of chemotherapy. Our aim was to compare GemDoc with Dox as first-line treatment of locally advanced/ metastatic STS.

Methods: Patients (pts) from 24 UK sites and 1 Swiss site were randomised to receive 6 cycles of Dox 75 mg/m^2 intravenously (IV) day 1 every 3 weeks, or Gem 675 mg/m^2 IV days 1 and 8 and Doc 75 mg/m^2 IV day 8 every 3 weeks (wks). Pts had locally advanced/metastatic STS, Trojani grade 2 or 3, disease progression prior to enrolment, no prior chemotherapy for sarcoma, no prior Dox, WHO performance status 0–2, age ≥ 13 years. Pts were stratified by age (≤ 18 or > 18 years) and histological subtype (uterine leiomyosarcoma [uLMS], synovial, pleomorphic, and other). Primary endpoint was progression free survival (PFS) rate (PFR) at 24 wks.

Results: From Dec 2010–Jan 2014, 257 pts were randomised (n = 129 Dox; n = 128 GemDoc). Median follow up was 19 months. 61% of pts were female; median age was 55 years. Baseline characteristics were balanced. Histology was 27% uLMS, 4% synovial, 12% pleomorphic, 56% other. PFR at 24 wks was 46.1% vs. 46.0%, median PFS was 23 vs. 24 wks, for Dox vs. GemDoc, but the hazard ratio (HR) was 1.28 (95% CI 0.98-1.67, P = 0.07) in favour of Dox. Median OS was 71 vs. 63 wks (HR = 1.07; 95% CI 0.77-1.49) for Dox vs. GemDoc. Although the PFS Kaplan-Meier curves did not violate the proportional hazards assumption (p = 0.53), they initially overlapped, and then separated after 24 wks in favour of Dox. Best response (CR/PR/SD) was 65.9% (Dox) vs. 58.6% (GemDoc). Mean dose intensity was 94.6% (Dox) vs. 83.3% (GemDoc). 46% (Dox) v 61% (GemDoc) of pts had at least one dose delay; 1 pt (2%) on Dox vs. 13 pts (16%) on GemDoc stopped treatment early due to toxicity.

Conclusions: Although the PFR at 24 wks was the same for Dox and GemDoc, the HR indicated superiority of Dox. Dox was less toxic and easier to deliver than GemDoc, and should remain standard first-line treatment for locally advanced/ metastatic STS.
Clinical trial information: ISRCTN07742377.

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Hormone-naïve Prostate Cancer

Studie: «Docetaxel and/or zoledronic acid for hormone-naïve prostate cancer: First overall survival results from STAMPEDE (NCT00268476).»

First Author: Nicholas David James, University of Warwick, Coventry, United Kingdom
 # 5001 Oral Abstract Session

Background: STAMPEDE is a randomised controlled trial using a novel multi-arm multi-stage design. It recruits men (pts) with high-risk locally advanced or metastatic prostate cancer (PCa) starting long-term hormone therapy (HT) for the first time. The trial initially assessed adding 1 or 2 of 3 treatment approaches to standard of care (SOC). We report primary survival results for 3 research comparisons that recruited through all their intermediate analyses: docetaxel (D), zoledronic acid (ZA) and the combination (D+ZA).

Methods: SOC was hormone therapy for ≥ 3 yrs; Radiotherapy (RT) was encouraged for N0M0 pts up to Nov-2011, then mandated; RT was optional for N+M0 pts. Stratified randomisation allocated pts 2:1:1:1 to SOC (control), SOC+D, SOC+ZA or SOC+D+ZA. 4 mg ZA was given for six 3-weekly cycles then 4-weekly until 2 yrs. D was given as 75 mg/m^2 for six 3-weekly cycles with prednisolone

10 mg daily. The primary outcome measure was survival (time from randomisation to death from any cause). Pairwise comparisons to control on survival for each research arm had 90% power at 2.5% 1-sided alpha for a hazard ratio of 0.75 requiring about 400 control arm deaths, accounting for 3 intermediate lack-of-benefit analyses on failure-free survival. Analyses used the Cox model of the logrank test, adjusted for stratification factors.

Results: From Oct-2005 to Mar-2013, 2,962 pts were randomised to the 4 arms. The groups were balanced with median age 65 yrs; 61% metastatic, 14% N/XM0, 22% N0M0; 93% diagnosed within 6 months of randomisation; median PSA 65 ng/ml. Median follow-up was 42 months. Grade 3-5 toxicity was reported for 31% SOC, 50% SOC+D, 32% SOC+ZA and 52% SOC+D+ZA. There were 405 deaths on the control arm (84% from PCa). The hazard ratio was 0.76 (95% CI 0.63, 0.91; p = 0.003) for SOC+D vs. SOC; 0.93 (95% CI 0.79, 1.11; p = 0.437) for SOC+ZA vs. SOC; and 0.81 (95% CI 0.68, 0.97; p = 0.020) for SOC+D+ZA vs. SOC. Median survival was increased by 10 months from 67 months on SOC to 77 months on SOC+D. Results in M0 and M1 disease will be shown.

Conclusions: Survival data from STAMPEDE show a clinically and statistically significant improvement in survival from adding docetaxel but not from adding zoledronic acid in men starting long-term hormone therapy for the first time.
Clinical trial information: NCT00268476.

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Prostate Cancer

Studie: «Acute toxicity and early quality of life after dose intensified salvage radiotherapy for biochemically recurrent prostate cancer after prostatectomy: First results of the randomized trial SAKK 09/10.»

First Author: Pirus Ghadjar, Department of Radiation Oncology, Charité Universitätsmedizin Berlin, Berlin, Germany
5038 Poster Session (Board #30)

Background: Patients (pts) with biochemical recurrence after radical prostatectomy may benefit from dose intensified salvage radiotherapy (RT) of the prostate bed. We performed a randomized phase III trial assessing dose intensification. In this first report we report acute toxicity and early quality of life (QoL).

Methods: Pts with biochemical recurrence but without evidence of macroscopic disease were enrolled in this randomized phase III trial. Pts were randomly assigned to either 64 Gy (32 daily fractions) or 70 Gy (35 daily fractions). Three-dimensional conformal RT (3D-CRT) or intensity-modulated RT (IMRT, or equivalent rotational techniques) were accepted techniques. The primary endpoint was freedom from biochemical recurrence. Secondary endpoints included acute toxicity according to the CTCAE v4.0 and QoL using the EORTC QLQ-C30 and PR25.

Results: We enrolled 350 pts between 02/2011 and 04/2014. Three pts withdrew consent and three were not eligible, resulting in 344 pts in the safety population. Thirty (8.7%) and two (0.6%) pts had grade 2 and 3 genitourinary (GU) baseline symptoms. Acute grade 2 and 3 GU toxicity was observed in 22 (13.0%) and 1 (0.6%) with 64 Gy and 29 (16.6%) and 3 (1.7%) with 70 Gy, being not significantly different (p =?0.2). Baseline grade 2 gastrointestinal (GI) toxicity was observed in 1 (0.6%) patient. No baseline grade 3 GI toxicity was observed. Acute grade 2 and 3 GI toxicity was observed in 27 (16.0%) and 1 (0.6%) with 64 Gy and 27 (15.4%) and 4 (2.3%) with 70 Gy, again not significantly different (p = 0.8). Changes in QoL were marginal. However, pts receiving 70 Gy reported a more pronounced and clinically relevant worsening in urinary symptoms (mean difference between arms 3.6, p = 0.02). There was no significant difference between 3D-CRT and IMRT/rotational techniques.

Conclusions: Dose-intensified salvage RT was associated with a low rate of grade 2 and 3 GU and GI toxicities. The impact of dose intensified salvage RT on QoL was marginal, with the exception of a worsening in urinary symptoms after 70 Gy.
Clinical trial information: NCT01272050.

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