Review papers ESMO/EHA/ESTRO 2019, presented by the mentees of the Young Oncology Academy 2019

The Swiss Group for Clinical Cancer Research (SAKK) launched the Young Oncology Academy, a mentoring program for young oncologists, in 2016. The program is aimed at residents at the beginning of their medical career with a clear focus on cancer medicine, hematology or radiooncology, who would like to actively contribute to clinical and translational research. In 2019, six mentees successfully concluded the program. As part of the program, the participants are to write a short review paper on the visited congress (ESMO, EHA or ESTRO 2019). The call for application for the Young Oncology Academy 2020 is open. Please find further information on the SAKK website: sakk.ch/researchers/young-oncology-academy.

Highlights of 2019 ESMO congress: lung cancer and mesothelioma

At the 2019 ESMO congress many interesting trials have been presented in the field of lung cancer and mesothelioma.

CheckMate-227[1,2]

The phase III CheckMate-227 trial included patients with stage IV non small cell lung cancer (NSCLC) who had received no prior treatment. Part 1 of the CheckMate-227 study consisted of 2 cohorts: patients with PD-L1 expression ≥1% (Part 1a) and <1% (Part 1b). In Part 1a, patients were randomized 1:1:1 to receive nivolumab plus low dose ipilimumab (1 mg/kg q6w), standard dose nivolumab, or platinum-based chemotherapy. In Part 1b, patients were assigned 1:1:1 to nivolumab plus ipilimumab, chemotherapy, or nivolumab plus chemotherapy. The independent co-primary endpoints of the study compared nivolumab plus ipilimumab versus chemotherapy in terms of progression free survival (PFS) in the high tumor mutational burden (TMB ≥10 mutations/Mb) population (results already published[3]) and overall survival (OS) in the PD-L1 ≥1% population. At the ESMO 2019 congress the latter co-primary endpoint was presented. Median OS with nivolumab and ipilimumab in the PD-L1 ≥1% population was superior to chemotherapy (17.1 vs. 14.9 months; HR: 0.79; 95% CI: 0.65–0.96; p=0.007). In an exploratory analysis of Part 1a, the median OS of single agent nivolumab was 15.7 months. In Part 1b (PD-L1 negative cohort), the combination of nivolumab and ipilimumab improved median OS from 12.2 months (chemotherapy) to 17.2 months. There were no new safety signals with the immunotherapy combination; grade 3/4 treatment-related adverse events were reported in 33%, 19%, and 36% of patients in the nivolumab plus ipilimumab, nivolumab, and chemotherapy arm, respectively. Interestingly, exploratory subgroup analysis did not reveal a predictive role of TMB.

Conclusion

Nivolumab plus ipilimumab is a new first-line treatment option, although its role in the context of combined immuno-chemotherapy has to be defined.

FLAURA[4]

The phase III FLAURA trial included previously untreated patients with locally advanced or metastatic NSCLC harboring a sensitizing *EGFR* mutation. Patients were randomized 1:1 to receive osimertinib or standard of care (SoC) TKI (erlotinib or gefitinib). Patients with disease progression under standard TKI were allowed to crossover to osimertinib. PFS as primary endpoint was significantly improved (median PFS 18.9 vs. 10.2 months) as previously published.[5] Both, objective response rate (ORR: 80% vs. 76%) and median duration

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of response (DoR: 17.2 vs. 8.5 months) were higher with osimertinib. At ESMO the final OS analysis was presented. Median OS was improved by 6.8 months with osimertinib. Median OS in the osimertinib arm was 38.6 months compared to 31.8 months in the SoC arm (HR: 0.799; 95% CI: 0.647–0.997; p=0.0462). Patients remained longer on osimertinib therapy (70% vs. 47% after 12 months) and time to first subsequent treatment was significantly prolonged with osimertinib (25.4 vs. 13.7 months). Cross-over to osimertinib occurred in 30% of patients. Importantly, 30% in both treatment arms received no subsequent anti-cancer therapy.

Conclusion

Osimertinib is the new SoC 1st line treatment for patients with a sensitizing *EGFR* mutation.

PROMISE-meso[6]

In the phase III study PROMISE-meso, patients with relapsed malignant pleural mesothelioma after platinum-based chemotherapy were randomized 1 : 1 to receive pembrolizumab or institutional choice of chemotherapy (gemcitabine, vinorelbine). Cross-over was allowed. PFS assessed by blinded independent central review was the primary endpoint. The study missed the primary endpoint. Median PFS with pembrolizumab was 2.5 months compared to 3.4 months in the chemotherapy arm. There was also no significant difference in OS (median OS 10.7 vs. 11.7 months). The substantially higher ORR with pembrolizumab (22% vs. 6%) did not translate into a longer DoR (4.6 months vs. 11.2 months).

Conclusion

Pembrolizumab monotherapy is not superior to standard chemotherapy in the 2nd line setting. Further studies are investigating combination therapies and the use of checkpoint inhibitors in earlier settings. ■

Authors:
Dr. med. **David König**
Medical Oncology
Cantonal Hospital Winterthur
PD Dr. med. **Sacha Rothschild**
University Hospital Basel

Literature:

1 Peters S et al.: Nivolumab (NIVO) + low-dose ipilimumab (IPI) vs platinum-doublet chemotherapy (chemo) as first-line (1L) treatment (tx) for advanced non-small cell lung cancer (NSCLC): CheckMate 227 part 1 final analysis. ESMO 2019, Abstr. #LBA4_PR **2** Hellmann MD et al.: Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. N Eng J Med 2019; doi: 10.1056/NEJMoa1910231 **3** Hellmann MD et al.: Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. N Engl J Med 2018; 378: 2093-104 **4** Ramalingam SS et al.: Osimertinib vs comparator EGFR-TKI as first-line treatment for EGFRm advanced NSCLC (FLAURA): final overall survival analysis. ESMO 2019, Abstr. #LBA5_PR **5** Soria JC et al.: Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. N Engl J Med 2018; 378: 113-25 **6** Popat S et al.: A multicentre randomized phase III trial comparing pembrolizumab (P) vs single agent chemotherapy (CT) for advanced pre-treated malignant pleural mesothelioma (MPM): results from the European Thoracic Oncology Platform (ETOP 9-15) PROMISE-meso trial. ESMO 2019, Abstr. #LBA91_PR

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ESMO highlights 2019: gastrointestinal malignancies

This year's ESMO congress was again a firework of exciting new data. Importantly, a variety of interesting and long awaited data on gastrointestinal malignancies were presented. We will hereby present three highly relevant studies.

Hepatocellular carcinoma (HCC): Checkmate 459 trial

In advanced hepatocellular cancer first line treatment options consist in VEGF-directed tyrosine kinase inhibition (TKI) with sorafenib or lenvatinib.[1] Immune checkpoint blockade showed promising results in a phase I/II trial.[2]

However, immunotherapy and TKI therapy have never been compared in a phase III study, which was the aim of the CheckMate 459 study.[3] 743 patients with previously untreated advanced HCC were randomized to receive nivolumab or sorafenib. Disappointingly, the primary endpoint overall survival was not significantly different (16.4 vs. 14.7; HR: 0.85;

p=0.0752). Nivolumab showed an objective response rate (ORR) of 15% vs. 7% with sorafenib. In patients with PD-L1 positive tumors (≥1%) ORR increased to 28% (20 patients) with nivolumab compared to 9% in the sorafenib group. Safety and quality of life analyses also favored the nivolumab group with the known low rate of grade 3/4 toxicity.

Even though overall survival was not superior over sorafenib, nivolumab showed clinically meaningful responses and long-term survival with a favorable safety profile. Due to the later separation of the survival curves, favoring nivolumab, final results of OS should be assessed after longer follow-up.

Meanwhile, results of the IMbrave 150 trial (atezolizumab/bevacizumab vs sorafenib; phase III) were announced in a press release, indicating the IO arm to be superior for OS and PFS.[4]

Locally advanced pancreatic cancer: NEOLAP trial

The majority of patients with newly diagnosed pancreatic ductal adenocarcinoma (PDAC) present in a locally-advanced or metastasized stage. The conversion of patients with unresectable, locally advanced PDAC using intensive induction therapy has shown to improve overall survival. The German multicenter phase II NEOLAP trial[5] compared induction chemotherapy of gemcitabine/nab-paclitaxel (G/nP) with sequential therapy of G/nP and FOLFIRINOX.

168 patients with locally advanced PDAC were randomized to receive 4 cycles G/nP versus 2 cycles G/nP and 4 cycles FOLFIRINOX, then both arms followed by surgery and another 3 cycles G/nP.

Due to the small sample size no significant difference was demonstrated neither in the resection rate (primary endpoint; 45.0 vs. 30.6%; p=0.135) nor in OS and PFS (secondary endpoints). However, the 15% difference in resection rate suggests a clinically meaningful benefit of an intensive induction therapy with G/nP followed by FOLFIRINOX. Moreover, the study design of this small, randomized trial was suboptimal, a randomization of induction chemotherapy of FOLFIRINOX versus G/nP would have been more meaningful. Overall, FOLFIRINOX appears to be more active as induction chemotherapy for locally-advanced PDAC. Indeed, large cohort studies have shown resections rates of up to 60%[6] in this setting.

Metastatic colorectal cancer (mCRC): BEACON trial

BRAF^{V600E} mutated mCRC represents a very aggressive phenotype with bad prognosis in about 10% of mCRC patients.[7] Clearly there is a need for targeted therapy after failure of first line therapy. The phase 3 trial BEACON[8] compared two targeted therapy regimes consisting of encorafenib, binimetinib and cetuximab (triplet) or encorafenib and cetuximab (doublet) with standard chemotherapy plus cetuximab. 665 previously treated mCRC patients were included. Both targeted treatment arms showed significant improvements in ORR (primary endpoint; 35% [triplet] and 29% [doublet] vs. 7%; p<0.0001) and overall survival (9.0 [triplet], 8.4 [doublet] vs. 5.4 months; HR: 0.52; p<0.001). Comparison between the both TKI arms were not possible at this early interim analysis. All three arms proved to be safe with tolerable rates of grade 3 toxicity, however, being higher in the triplet compared to the doublet arm. Due to these positive results, targeted doublet or triplet therapy should be considered a new standard of care in this patient subset. ■

Author:
Dr. med. **Lorenz Bankel**
Medical Oncology
University Hospital Zurich

Literature:

1 Vogel A et al.: Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2019; 30: 871-3 **2** El-Khoueiry AB et al.: Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. Lancet

2017; 389: 2492-502 **3** Yau T et al.: CheckMate 459: a randomized, multi-center phase III study of nivolumab (NIVO) vs sorafenib (SOR) as first-line (1L) treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC). ESMO 2019; Abstr. #LBA38_PR **4** Ltd, H.-L. R., Media Release: Roche's Tecentriq in combination with Avastin increased overall survival and progression-free survival in people with unresectable hepatocellular carcinoma. (2019) **5** Kunzmann V et al.: Conversion rate in locally advanced pancreatic cancer (LAPC) after nab-paclitaxel/gemcitabine- or FOLFIRINOX-based induction chemotherapy (NEOLAP): final results of a multicenter randomised phase II AIO trial. ESMO 2019, Abstr. #6710 **6** Hackert T et al.: Locally advanced pancreatic cancer: neoadjuvant therapy with folfirinox results in resectability in 60% of the patients. Ann Surg 2016; 264: 457-63 **7** Tran B et al.: Impact of BRAF mutation and microsatellite instability on the pattern of metastatic spread and prognosis in metastatic colorectal cancer. Cancer 2011; 117: 4623-32 **8** Tabernero J et al.: Encorafenib plus cetuximab with or without binimetinib for BRAF V600E–mutant metastatic colorectal cancer: expanded results from a randomized, 3-arm, phase III study vs the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). ESMO 2019; Abstr. #LBA32

ESMO highlights 2019: genitourinary tumors

At this year's annual ESMO congress many interesting trial results have been presented in the field of genitourinary oncology. Here, we highlight four trials that are most important for daily practice.

RADICALS trial

In the RADICALS trial the effect of adjuvant radiotherapy vs. early salvage radiotherapy after radical prostatectomy was investigated.[1] The primary endpoint – freedom from distant metastases – has not been reached yet, but preliminary results regarding biochemical recurrence-free survival were currently presented. Patients after radical prostatectomy (with at least one of the following criteria: pT3/4, Gleason score 7–10, preoperative PSA ≥10 ng/ml or positive surgical margins) with a postoperative PSA ≤0.2 ng/ml were randomized to adjuvant or early salvage radiotherapy (administered in case of consecutive rises and PSA >0.1 mg/ml). Of 1396 recruited patients the majority had locally advanced disease (pT3/4: 75%) and/or positive surgical margins (R1: 63%). After a median follow up of 5 years no benefit of adjuvant radiotherapy was found with regards to biochemical recurrence (HR: 1.1; 95% CI: 0.81–1.49; p=0.56). In the salvage arm 63% of patients didn't require treatment. The preliminary results from the RADICALS trial therefore support the concept of early salvage radiotherapy by which >60% of patients can be spared from radiotherapy.

CARD trial

Ronald de Wit presented the results from the CARD trial, comparing cabazitaxel to treatment with a new hormonal agent (NHA; abiraterone or enzalutamide) in the third line setting for metastatic castration-resistant prostate cancer (mCRPC).[2] Patients with mCRPC having been treated with docetaxel and who progressed on NHA within 12 months were randomized to Cabazitaxel (n=129) or the NHA that had not been previously administered (n=126). In the cabazitaxel and NHA-groups, median age was ≥75 years in 35% and 27%, and tumor progression was clinical in 67% and 71% respectively. The primary endpoint of radiographic progression-free survival was much improved in the cabazitaxel-group (8 months; 95% CI: 5.7–9.2) compared to the NHA allocation (3.7 months; 95% CI: 2.8–5.1) and statistically significant (HR: 0.54; 95% CI: 0.40–0.73; p<0.0001). Median overall survial (OS) was also significantly improved with 13.6 vs. 11.0 months (HR: 0.64; 95% CI: 0.46–0.89; p=0.0078). The CARD trial therefore marks a practice changing study making cabazitaxel the new third line standard for mCRPC patients progressing after docetaxel and on a NHA within 12 months.

PROFOUND trial

Treatment with a PARP-inhibitor in mCRPC patients with DNA repair gene alterations demonstrated interesting efficacy in a small phase II study.[3] Based on these results, the PROFOUND trial evaluated the efficacy of the PARP-inhibitor olaparib vs. NHA in mCRPC patients with homologous recombination repair (HRR) alterations, who progressed after NHA-treatment.[4] In total, 632 patients were recruited and allocated to cohort A (*BRCA1*, *BRCA2* and *ATM* alterations; n=245) and cohort B (any other HRR gene alteration; n=142). Patients from both cohorts were randomized 2:1 to olaparib or NHA (abiraterone or enzalutamide at the physician's choice). All patients were preatreated with a NHA, of which 19% had received both abiraterone and enzalutamide, and 65% had previously received docetaxel, cabazitaxel or both. In cohort A the primary endpoint of radiographic progression free survival was more than doubled with olaparib (HR: 0.34; 95% CI: 0.25–0.47; p<0.0001). The effect was most pronounced in patients with *BRCA2*-mutations whereas patients with other HRR alterations had less benefit. PROFOUND marks the first positive biomarker-selected phase III trial in mCRPC, supporting HRR testing in mCRPC-patients progressing after NHA to select for olaparib-sensitivity.

IMvigor130 trial

The IMvigor130 trial randomized 1213 platinum-eligible patients with untreated locally advanced or metastatic urothelial carcinoma to standard of care chemotherapy of platinum/gemcitabine, monotherapy with the anti-PD-L1 inhibitor atezolizumab or the combination of platinum/gemcitabine and atezolizumab. Interestingly, a substantial number of patients re-

ceived carboplatin instead of cisplatin based on the physician's choice despite fulfilling Galsky criteria for ciplatin-eligibility. It is unclear, what impact this has on the trial results. The primary endpoint of progression-free survival (PFS) for the combination-treatment vs. platinum-based chemotherapy was reached and was positive (HR: 0.82; 95 % CI: 0.70–0.96). The combination-treatment improved median PFS from 6.3 (6.2–7.0) months to 8.2 (6.5–8.3) months. In an interim analysis, OS was numerically improved for the combination of chemotherapy/atezolizumab (16.0 vs. 13.4 months) but did not meet the prespecified statistical threshold. Longer follow-up will reveal if patients with metastatic urothelial carcinoma may have improved survival using the combination of chemotherapy and atezolizumab as first line treatment. ■


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Authors:
Dr. med. **Karim Saba**[1]
PD Dr. med. **Richard Cathomas**[2]
[1] Department of Urology
[2] Department of Oncology
Cantonal Hospital Graubünden, Chur

Literature:

1 Parker C et al.: Timing of radiotherapy (RT) after radical prostatectomy (RP): first results from the RADICALS RT randomised controlled trial (RCT) [NCT00541047]. ESMO 2019, Abstr. LBA49_PR **2** de Wit R et al.: Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. N Engl J Med 2019, doi: 10.1056/NEJMoa1911206 **3** Mateo J et al.: DNA-repair defects and olaparib in metastatic prostate cancer. N Engl J Med 2015; 373: 1697-708 **4** Hussain M et al.: PROfound: phase III study of olaparib versus enzalutamide or abiraterone for metastatic castration-resistant prostate cancer with homologous recombination repair gene alterations. ESMO 2019, Abstr. #LBA12_PR

EHA 2019 updates – multiple myeloma

The treatment of relapsed and refractory multiple myeloma is a challenge. The EHA congress 2019 provided several highlights on this topic.

COLUMBA trial: intravenous versus subcutaneous administration of daratumumab

Daratumumab, a monoclonal antibody targeting CD38, has proven efficacy in multiple myeloma across all lines of therapy. Similar to the anti-CD20 antibody rituximab the intravenous administration lasts several hours; in particular, the first infusion takes an average of seven hours.[1] In contrast, a subcutaneous infusion will only take 3–5 minutes.

The Columba study presented by Maria Victoria Mateos, is a randomised phase III study, which compared the intravenous (IV) versus subcutaneous (SC) administration of daratumumab in patients with relapsed or refractory multiple myeloma (R/R MM).[2] 522 patients with R/R MM and at least 3 prior lines of therapy were enrolled and randomised 1 : 1 to receive either daratumumab SC (1800 mg) or daratumumab IV (16 mg/kg). The overall response rate (ORR) and the maximum trough concentration, as the two primary end-points, were comparable between the subcutaneous and intravenous administration of daratumumab (41,1 % vs. 37,1 % ORR and maximum trough concentration dara-SC/dara-IV: 107,93 %).

In addition, the safety profile between two routes of administration was similar. Daratumumab SC was even associated with a significantly lower rate of infusion-related reactions (12,7 % for SC vs. 34,5 % for IV; $p < 0{,}0001$).

In conclusion the subcutaneous administration of daratumumab is both safe and effective and due to the shorter administration time convenient for patients and health care professionals.

ICARIA-MM trial: isatuximab plus pomalidomide and dexamethasone a new therapy option in patients with R/R MM?

The ICARIA-MM trial presented by Paul Richardson from the Dana-Farber Cancer Institute focused on isatuximab, another anti-CD38 monoclonal antibody.[3] The function of isatuximab is in many ways similar to daratumumab. However, isatuximab has less complement-dependent cytotoxicity than daratumumab. Therefore, perhaps isatuximab leads to less infusion-related reactions and has shorter infusion time than daratumumab.

In the ICARIA trial, an international phase III study, 307 patients with R/R MM and at least 2 prior lines of therapy were randomised 1:1 to receive either isatuximab together with pomalidomide and low dose dexamethasone (Isa-Pd) or pomalidomide and low dose dexamethasone alone (Pd).[4]

The median progression free survival was significantly higher in the patient cohort receiving Isa-Pd (11,53 months for the Isa-Pd arm vs. 6,47 for the Pd arm, (95% CI: 0,44–0,81; p=0,001). In line with these findings, the overall response rate (ORR) was also significantly higher with 60,4% in the Isa-PD arm versus 35,3% in the Pd arm.

Overall, the safety profile was manageable, despite a higher rate of neutropenia and infections in the cohort with isatuximab.

In summary isatuximab in combination with pomalidomide and dexamethasone is a new therapeutic option in R/R MM, but open questions remain: Is isatuximab still effective for myeloma patients who are refractory to daratumumab and/or elotuzumab? Can isatuximab be given after treatment with daratumumab?

AMG 420, an anti-BCMA bispecific T-cell engager (BiTE®) immunotherapy

B cell maturation antigen (BCMA) is a cell surface receptor, which belongs to the tumor necrosis factor receptor (TNFR) superfamily and is almost exclusively expressed on plasmacells and plasmablasts.[5] In the last few years multiple immunotherapies directed against BCMA haven been developed, such as BCMA CAR-T or BCMA-BiTE®. A BCMA-BiTE® links with CD3 on T-cells on one side and with BCMA on plasma cells on the other side.

At the EHA, Max Topp presented results of a first-in-human phase I dose escalation study with the anti-BCMA BiTE® AMG 420. Primary endpoints were dose limiting toxicity and maximum tolerated dose.[6]

AMG 420 was given by continuous infusion in 6-week cycles for 5 cycles or until disease progression (PD) or toxicity. Dose limiting toxicity was reached in three of 42 patients and in two cases at a dose of 800 μg/d. The maximum tolerated dose was thus 400 μg/d.

Overall 13 of 42 patients responded to the treatment with the highest response rate of 70% at a dose of 400 μg/d (7 of 10 patients). Therefore, the recommended dose for further investigation is 400 μg/d. ■

Authors:
Dr. med. **Katharina Baur**
University Hospital Basel
PD Dr. med. **Urban Novak**
Inselspital, Universitätsspital Bern

Literature:

1 Darzalex® (daratumumab) injection, for intravenous use [package insert]. Janssen Biotech, Inc., Horsham, PA, 2019 **2** Mateos MV et al.: Randomized, open-label, non-inferiority, phase 3 study of subcutaneous (sc) versus intravenous (iv) daratumumab (dara) administration in patients with relapsed or refractory multiple myeloma: COLUMBA. EHA 2019, Abstr. #S823 **3** Richardson PG et al.: Isatuximab plus pomalidomide/dexamethasone versus pomalidomide/dexamethasone in relapsed/refractory multiple myeloma: ICARIA phase III study design. Future Oncol 2018; 14(11): 1035-47 **4** Richardson PG et al.: A phase 3 randomized, open-label, multicenter study of isatuximab, pomalidomide, and low-dose dexamethasone vs pomalidomide and low-dose dexamethasone in relapsed/refractory multiple myeloma (RRMM). EHA 2019, Abstr. #S824 **5** Tai YT, Anderson KC: B cell maturation antigen (BCMA)-based immunotherapy for multiple myeloma. Expert Opin Biol Ther 2019; Jul 11: 1-14 **6** Topp M et al.: Evaluation of AMG 420, an anti-BCMA bispecific T-cell engager (BiTE®) immunotherapy, in R/R multiple myeloma (MM) patients: updated results of a first-in-human (FIH) phase 1 dose escalation study. EHA 2019, Abstr. #S825

ESTRO highlights 2019: therapeutic implications

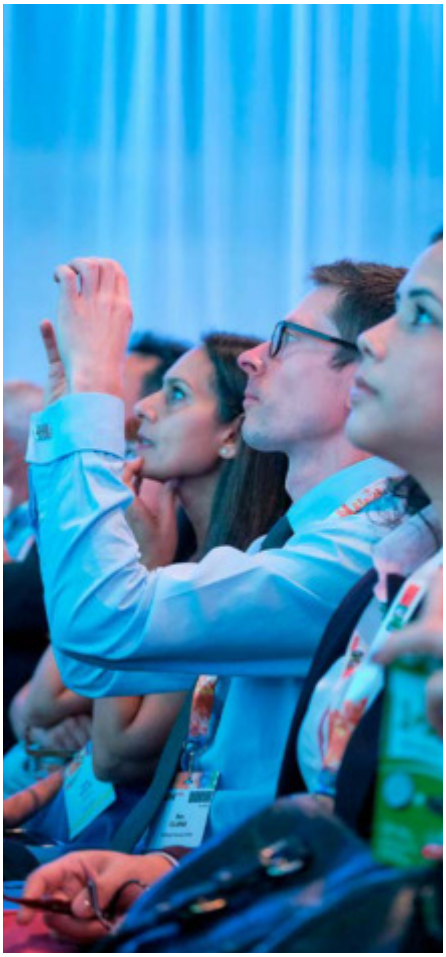
The European Society of Radiation Oncology (ESTRO) was founded in 1980. In 2019 the 38th edition came about in achieving the attendance of more than 6000 participants from 100 countries. I review three papers focussing on the effectiveness combining different drugs as targets or antibiotics with radiation and improving patient's quality of life shortening treatment time.

Hypofractionated vs. conventional radiotherapy for prostate cancer: 7-years results from the HYPRO trial

The study is based on improving efficacy of treatment in prostate cancer using moderate hypofractionated radiotherapy (HF).[1] The use of linear-quadratic model suggests that HF schema will produce less toxicity and will be more effective in prostate cancer. HYPRO is a randomized phase III trial investigating in 804 patients the superiority of hypofractionated versus conventionally fractionated (CF) radiotherapy for patients with intermediate- or high-risk, localized, prostate cancer, actualized at 7-years follow-up. Patients were randomized to HF (64.6 Gy in 19 fr) or CF (78 Gy in 39 fr). The primary endpoint was relapse-free survival (RFS) at 7 years. The results indicate that RFS was 71.7 % (95 % CI: 66.4–76.4) for HF versus 67.6 % (95 % CI: 62–72.5) for CF (p = 0.52). No statistical significant evidence of heterogeneity across subgroups was observed. Local RFS sub-analysis reflected a significant interaction between treatment arm and Gleason score ≥ 8. HF arm did not translate in superior tumor control. Under these results, HF cannot be implemented as new standard of care. In my view, after several RCTs trials it has been demonstrated that moderate HF confers similar prostate-cancer-control outcomes with similar rates of late toxicity. Considering the convenience of the patients and the cost of treatment, both options can be discussed with patients.

Stereotactic radiotherapy (SRT) for oligoprogressive NSCLC: clinical scenarios affecting survival

Disease outcome as well as toxicity is not well known in combination between SRT and target treatment. The TOASTT trial is a DEGRO initiative multicentric registry. It evaluated in 108 patients SRT of 192 lesions undertaken in 16 clinics.[2] OS, PFS, LC and time to systemic therapy-switch after SRT were analysed. Concurrent treatment was in 60 % ALK- or EGFR-TKI, in 31 % PD-L1/PD-1 inhibitors and in 8 % bevacizumab. Patients were divided in SRT of ≤ 5 metastases without additional disease, SRT of ≤ 5 progressive



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metastases with controlled disease of all other metastases and SRT of ≤ 5 metastases with mixed response or uncontrolled disease. The results demonstrate that LC after SRT was excellent in all groups, with limited severe toxicity. Significant improve in OS for patients with limited progressive disease and PFS especially good in the first group was observed. A large number of patients could continue the same systemic treatment 1 year after SRT (86 %, 47 % and 39 %). The majority had oligometastatic recurrence treated most frequently with an ablative treatment. The abstract suggests that despite good results we need prospective trials. In my opinion, we must be careful to know the implication of radiation localisation and time between both.

Gut microbiota SCFAs (short chain fatty acids) modulate dendritic cell antigen presentation and impact in radiotherapy

The role of microbiota in immunomodulation can compromise the response to radiation treatment promoting specific T-cell subsets. Vancomycin was used here to evaluate this impact.[3] It was observed that vancomycin potentiates the RT-induced anti-tumor immune response and tumor growth inhibition in a melanoma and lung tumor model. The synergism between vancomycin-RT was dependent on TAA (tumor-associated antigens) cross presentation to cytolytic CD8+ T-cells and on IFN-gamma. Vancomycin treatment increases overall and well-specific T-cells infiltration in tumors and decreases the tumor draining lymph nodes. Supplementation of butyrate (SCFAs produced by microbial fermentation) inhibited antigen presentation and prevent vancomycin-RT synergy. In conclusion, depletion of vancomycin sensitive bacteria enhances the anti-tumor activity of RT, which has relevant clinical implications. To my mind, the implication from this work is that inhibitors of SCFA could potentially be delivered in combination with radiation to serve as radiosensitizers. ■

Authors:
Dr. med. **Olalla Santa Cruz**[1]
PD Dr. med. **Paula Tsoutsou**[2]
Prof. Dr. med. **Stephan Bodis**[3]
[1] Radiation Oncology Department
Réseau Hospitalier Neuchâtelois
La Chaux-de-Fonds
[2] Radiation Oncology Department HUG
Hôpitaux Universitaires de Genève
[3] Center for Radiation Oncology KSA-KSB
Cantonal Hospital Aarau

Literature:

1 Incrocci L et al.: Hypofractionated vs conventional radiotherapy for prostate cancer: 7 yr results from the HYPRO-trial. ESTRO 2019, Abstr. #OC-0272 **2** Kroeze S et al.: Stereotactic radiotherapy for oligoprogressive NSCLC: clinical scenarios affecting survival. ESTRO 2019, Abstr. #OC-0059 **3** Facciabene A et al.: Gut microbiota SCFAs modulate dendritic cell antigen presentation and impact radiotherapy. ESTRO 2019, Abstr. #OC-0331