Young Oncology Academy 2022

Welche Daten für den onkologischen Nachwuchs spannend waren

Das Kernstück in der Nachwuchsförderung der Schweizerischen Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK) ist die Young Oncology Academy (YOA), ein Förderungs- und Mentor*innenprogramm für junge Onkolog*innen. Das Programm richtet sich an Assistenzärzt*innen. Als Teil der Academy besuchen die Teilnehmenden einen grossen Kongress und fassen relevante klinische Daten zusammen.

ESMO 2022 highlights on prostate and urothelial cancer

© zVg

Luca Afferi (29) ist Assistenzarzt an der Klinik für Urologie am Luzerner Kantonsspital LUKS. Er war 2022 Mentee der SAKK Young Oncology Academy. Sein Fazit zur Academy: «Die Young Oncology Academy war für mich eine einzigartige Gelegenheit, ein besserer Arzt und Forscher zu werden, meine Präsentationsfähigkeiten zu verbessern, mein Netzwerk mit Kollegen verschiedener Disziplinen in der ganzen Schweiz zu erweitern und neue wissenschaftliche Kooperationen einzugehen.»

In the following summary we present two of the most relevant abstracts on prostate and urothelial cancer presented at the ESMO 2022 congress.

Duration of androgen deprivation therapy after radical prostatectomy and radiation therapy: results from the RADICALS-HD study

RADICALS-HD was a phase III trial enrolling patients with prostate cancer (PCa) at high risk of relapse after radical prostatectomy.[1] Patients were initially randomized 1:1 to either adjuvant or salvage radiation therapy (RT), and subsequently 1:1:1 to either no androgen deprivation therapy (ADT), 6 months of ADT or 24 months of ADT. For several reasons, this complex randomization was soon replaced by a 2 arm 1:1 randomization (figure 1).[2] Patients were either randomized to no ADT vs 6 months ADT, or 6 months ADT vs 24 months ADT. The primary endpoint was metastasis-free survival (MFS). In the part of the study evaluating no vs 6 months ADT, 1480 patients were enrolled; around 60% of patients had ypT3/4, 3% ypN1 and 11% Gleason score (GS) ≥ 8 PCa. 10-years MFS was 79% in the no ADT vs 80% in the 6 months ADT arm (HR: 0.89; 95%: CI 0.69–1.14; p-value 0.35). In the part of the study evaluating 6 months ADT vs 24 months ADT, 1523 patients were enrolled; approximately 72% of patients had ypT3/4, 8% ypN1 and 29% GS ≥ 8 PCa. 10-years MFS was 72% in the 6 months ADT vs 78% in the 24 months ADT arm (HR: 0.77; 95% CI: 0.61–0.97; p-value 0.03).

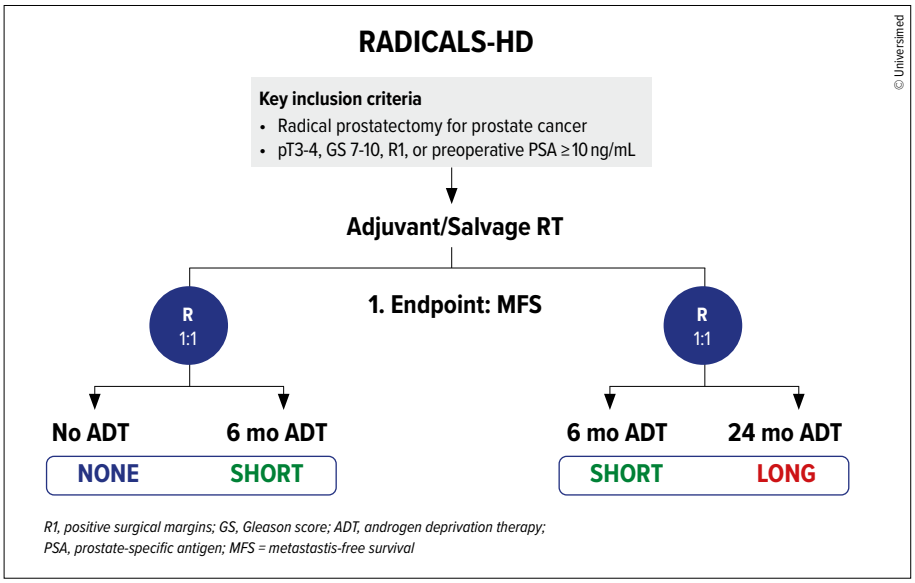

Fig. 1: Trial design of the RADICALS-HD study. Modified from Parker et al.[1]

The authors concluded that 24 months ADT increases MFS in PCa patients with risk factors for relapse receiving either adjuvant or salvage RT in comparison with 6 months ADT. Data on overall survival are still immature and awaited to draw definitive conclusions.

Enfortumab Vedotin (EV) in combination with pembrolizumab in locally advanced or metastatic urothelial cancer: the EV-103 Cohort K study

The first line treatment for patients with cisplatin-ineligible, locally advanced or metastatic urothelial cancer (la/mUC) is represented by carboplatin-gemcitabine or, in selected cases, immunotherapy (atezolizumab or pembrolizumab).[3] However, modest overall response rates (ORR) and overall survival (OS) from both therapies urge the need for new treatments.[3]

EV-103 Cohort K was a phase II randomized non-comparative trial evaluating the efficacy of EV monotherapy or in combination with pembrolizumab (pembro) in cisplatin-ineligible la/mUC.[4] A total of 149 patients were randomized 1:1 to EV (1.25 mg/kg) as monotherapy on days 1 and 8 every 3 weeks or EV with pembro (200 mg day 1) (figure 2). The primary endpoint was ORR by blinded independent central review. The confirmed ORR was 64.5% for EV/pembro combination compared to 45% for EV monotherapy. Moreover, 85.7% of the ORRs from EV/pembro were recorded in the first 9 weeks from the beginning of therapy and 97% of patients receiving EV/pembro had some reduction in tumor volume. The ORR was independent from PD-L1 expression. Most common treatment related adverse events (TRAEs) were fatigue, peripheral sensory neuropathy and skin reactions. Serious and lethal TRAEs occurred in 23.7% and 3.9% patients in the EV/pembro arm vs 15% and 2.7% in the EV monotherapy group, respectively. Nonetheless, the main reason for suspending treatment was disease progression and not TRAEs.

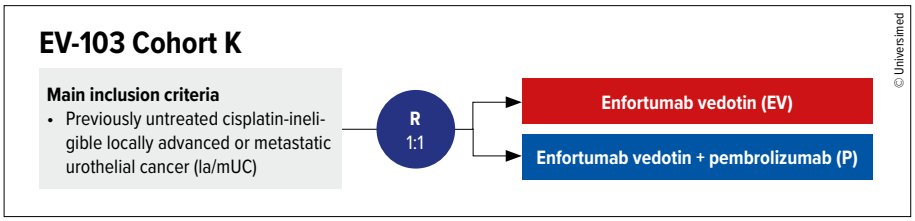

Fig. 2: Trial design of the EV-103 Cohort K. Modified from Rosenberg et al.[4]

The authors concluded that the combination of EV and pembro leads to a high ORR and rapid responses in patients with cisplatin-ineligible la/mUC. Therefore, this combination treatment has the potential to become the first line therapy of choice in this patients' population. Definitive results are expected to derive soon from an ongoing phase III trial (EV-302) assessing the combination of EV and pembro compared to platinum-based chemotherapy. ■

Authors:
Dr. med. **Luca Afferi**[1]
PD Dr. med. **Richard Cathomas**[2]
[1] Department of Urology
Luzerner Kantonsspital, Lucerne
[2] Division of Oncology/Hematology,
Kantonsspital Graubünden, Chur

Literature:
1 Parker CC et al.: ESMO 2022; Abstr. #LBA9 **2** Parker CC et al.: Clin Oncol (R Coll Radiol) 2022; 34(9): 593-7 **3** Powles T et al.: Ann Oncol 2022; 33(3): 244-58 **4** Rosenberg JE et al.: ESMO 2022; Abstr. #LBA73

ESMO highlights 2022 in gynecological cancer: Are we curing ovarian cancer patients?


© fotostudio_charlottenburg

Bich Doan Nguyen-Sträuli (35) arbeitet im Universitätsspital Zürich, an der Universität Zürich und am Institute of Molecular Health Sciences der ETH Zürich. Ihre Spezialgebiete sind gynäkologische Onkologie, Flüssigbiopsie und zirkulierende Tumorzellen. Sie hat an der Young Oncology Academy teilgenommen, weil es «eine Gelegenheit ist, über den Tellerrand zu schauen, interessante Menschen kennenzulernen und seine Kenntnisse zu vertiefen».

This year's congress provided overall survival (OS) results from the SOLO-1/GOG 3004 and PAOLA-1/ENGOT-ov25 trials investigating olaparib (ola) alone and in combination with bevacizumab (bev) as maintenance therapy in patients with advanced ovarian cancer (AOC).

Based on the results of randomized phase III trials, poly(adenosine diphosphate-ribose) polymerase inhibitors (PARPi) have been approved as a new standard of care in AOC and have revolutionized the way patients are treated in the front-line[1–4] and recurrent setting.[5–7] Currently, ola, niraparib, ola plus bev and bev demonstrated significant improvements in progression-free survival (PFS) and are approved for first-line maintenance therapy.[1,3,4,8]

SOLO-1/GOG 3004 trial

The results of SOLO-1 at 5 years showed that first-line maintenance therapy with ola substantially extended PFS in patients with newly diagnosed AOC with *BRCA* mutation (BRCAm).[1] OS analysis after 7-years of follow-up (FU) is a clinically relevant time point and the longest FU for any PARPi in the first-line setting. Patients with newly diagnosed AOC with *BRCA*m who had a clinical response to platinum-based chemotherapy were randomized to receive either ola (n=260) or placebo (n=131) for 2 years or until disease progression. The hazard ratio for OS was 0.55 (95% CI: 0.40–0.76), not achieving statistical significance (p=0.0004 [p<0.0001 required]).

It is worth acknowledging that 90 % of patients stopped ola treatment at 2 years and that in the subsequent 5 years only 33 % of patients died in the ola arm versus 53.5 % in the placebo cohort. Importantly, 45.3 % versus 20.6 %, respectively, had not received a first subsequent treatment suggesting that there might be cure for some AOC patients.

PAOLA-1/ENGOT-ov25 trial

This phase III trial compared maintenance ola + bev with placebo + bev in patients with newly diagnosed AOC who had received first-line standard-of-care treatment including bev regardless of *BRCA*m. In the primary analysis, ola + bev demonstrated a significant PFS benefit over placebo + bev (HR: 0.59; 95 % CI: 0.49–0.72; p<0.001), mainly in patients with HRD+ tumors (HR: 0.33; 95 % CI: 0.25–0.45). The final analysis investigated whether this translated into an OS advantage at 5 years. After a median FU of 61.7 months in the ola + bev arm and 61.9 months in the placebo + bev arm, median OS was 56.5 months vs 51.6 months, respectively (HR: 0.92; 95 % CI: 0.76–1.12; p=0.4118). OS rates at 5 years were 47.3 % with the addition of ola compared to 41.5 % with placebo.

The power of this study is shown in patients with HRD+ tumors where the addition of ola to bev reduced the risk for death by 38 % (HR: 0.62; 95 % CI: 0.45–0.85), with a 5-year OS of 65.5 % with the combination regimen and 48.4 % with placebo. This benefit was consistent in patients harboring a *BRCA*m (5-year OS, 73.2 % vs 53.8 %, respectively; HR: 0.60; 95 % CI: 0.39–0.93). However, no statistically significant benefit was seen in patients without *BRCA*m (5-year OS, 54.7 % vs 44.2 %; HR: 0.71; 95 % CI: 0.45–1.13), nor in HRD- patients (5-year OS, 32.3 % vs 25.7 %, respectively; HR: 1.19; 95 % CI: 0.88–1.63).

Conclusion

Ola (+/- bev) led to a clinically meaningful benefit in OS in patients with AOC and HRD+ (with and without BRCAm). The authors in both trials support the use of ola (and bev) in BRCAm (and HRD+) AOC. The survival data confirm the value of biomarker directed first-line maintenance therapy with ola.

Authors:
Dr. med. **Bich Doan Nguyen-Sträuli**[1]
Dr. med. **Francesca Caparrotti**[2]
[1] Gynecologic Oncology
University Hospital Zurich
[2] Radio-Oncology
Clinique Générale-Beaulieu
Swiss Medical Network, Geneva

Literature:

1 Moore K et al.: N Engl J Med 2018; 379: 2495-505 **2** Monk BJ et al.: J Clin Oncol 2022; 40: 3952-64 **3** González-Martín A et al.: N Engl J Med 2019; 381: 2391-402 **4** Ray-Coquard I et al.: N Engl J Med 2019; 381: 38: 2416-28 **5** Andres P et al.: J Clin Oncol 2020; 38(15_Suppl): 6002 **6** Coleman RL et al.: Lancet 2017; 390: 1949-61 **7** Mirza MR et al.: N Engl J Med 2016; 375: 2154-64 **8** Perren TJ et al.: N Engl J Med 2011; 365: 2484-96

ESMO highlights of the year 2022 – lung cancer


© KSSG

Kira-Lee Koster (35) ist an der Klinik für Medizinische Onkologie und Hämatologie im Kantonsspital St. Gallen tätig und interessiert sich besonders für die Gebiete Thoraxmalignome und Phase-I-Studien. Ihre Meinung zur Young Oncology Academy: «Die YOA bietet die einmalige Möglichkeit, Kolleg*innen mit Forschungsinteresse zu treffen, sich auszutauschen und ein Netzwerk aufzubauen, welches hoffentlich weit über die YOA hinaus besteht und wächst. Ich bin sehr froh, dass ich dabei sein durfte.»

We selected two studies in the field of lung cancer presented at this year's ESMO congress as highlights of the year. Both studies deal with targeted therapies in metastatic non-small cell-lung cancer (NSCLC).

The CodeBreaK 200 phase III study compared sotorasib versus docetaxel in patients with previously treated metastatic NSCLC that harbour a *KRAS* G12C mutation.[1] In the previous phase I/II CodeBreaK 100 study in metastatic *KRAS* G12C mutated NSCLC sotorasib used in 2nd–4th line showed an impressive objective response rate (ORR) of 37.1 % (95 % confidence interval [CI]: 28.6–46.2), and a progression-free survival (PFS) and overall survival (OS) of 6.8 months (95 % CI: 5.1–8.2) and 12.5 months (95 % CI: 10.0 – could not be evaluated), respectively.[2]

CodeBreaK 200 is the confirmatory phase III trial, comparing sotorasib to docetaxel, the standard of care in 2nd line, after progression to platinum and/or immunotherapy-based chemotherapy.[1] The study met its primary endpoint of PFS by blinded independent central review (BICR) with a hazard ratio (HR) of 0.66 (95 % CI: 0.51–0.86) for sotorasib in comparison to docetaxel (p=0.002). The median PFS for sotorasib is 5.6 months (95 % CI: 4.3–7.8) versus 4.5 months (95 % CI: 3.0–5.7) for docetaxel. The tumour response by BICR is also superior for sotorasib with an ORR of 28.1 % (95 % CI: 21.5–35.4) versus 13.2 % (95 % CI: 8.6–19.2) for docetaxel (p<0.001).

Although a significant PFS benefit was reported, no OS benefit could be demonstrated (HR: 1.01; 95 % CI: 0.77–1.33; p=0.53). However, the study was not powered to detect a statistically significant difference. The lack of OS benefit might be partly explained by crossover: 34 % of patients in the docetaxel arm received a subsequent KRAS G12C inhibitor.

The safety profile of both drugs is in the known range and revealed no new safety issues. The additionally presented patient-reported outcomes global health status, physical functioning and dyspnoea were superior for sotorasib, whereas there was no significant difference regarding cough and chest pain.

In our conclusion, sotorasib is a well-tolerated treatment alternative in previously treated *KRAS* G12C mutated NSCLC demonstrating a PFS benefit, better ORR and less toxicity, but one has to bear in mind that no OS benefit could be demonstrated.

Secondly, we would like to present the first results of the INSIGHT 2 phase II study, investigating the combination of osimertinib and tepotinib in *EGFR* mutated NSCLC with acquired resistance to 1st line osimertinib and harbouring a *MET* amplification as mechanism of resistance.[3]

The primary objective of this study was ORR by an independent review committee (IRC). A confirmed ORR of 54.5% (95% CI: 32.2–75.6) was reported in patients with *MET* amplification detected by central FISH on tumour biopsy with ≥9 months' follow-up. In comparison, an ORR of 8.3% (95% CI: 0.2–38.5) was reported in the tepotinib monotherapy arm with *MET* amplification detected by central FISH on tumour biopsy and ≥6 months' follow-up.

In this study, no new safety issues have been raised regarding the two substances. In our conclusion, the combination of osimertinib and tepotinib seems to be very active in *EGFR* mutated NSCLC progressing on 1st line osimertinib with *MET* amplification as mechanism of resistance. Furthermore, this study addresses a high unmet need, as there are no clear recommendations on how to treat patients progressing on osimertinib.

Authors:
Dr. med. **Kira-Lee Koster**[1]
Prof. Dr. med. **Miklos Pless**[2]
[1] Department of Medical Oncology and Haematology
Cantonal Hospital St. Gallen
[2] Department of Medical Oncology
Cantonal Hospital Winterthur

■15

Literature:

1 Johnson ML et al.: Ann Oncol 2022; 33: S1417-S1418
2 Skoulidis F et al.: N Engl J Med 2021; 384(25): 2371-81
3 Mazieres J et al.: Ann Oncol 2022; 33: S1419-S20

NEWS

Krebs und hochverarbeitete Lebensmittel

Eine Studie stellte einen Zusammenhang zwischen dem Konsum hochverarbeiteter Lebensmittel und dem Krebsrisiko fest.[1] Finanziert wurde sie vom World Cancer Research Fund und von Cancer Research UK. Die Forschenden stammen vom Imperial College London.

Die Ernährungsweise von 197 426 Menschen (40–69 Jahre) wurde über drei Jahre mithilfe der UK Biobank protokolliert. Der Konsum hochverarbeiteter Nahrungsmittel (UPF) wurde über den prozentualen Anteil des gesamten Nahrungskonsums in Gramm angegeben. Diese Angaben wurden zusammen mit dem Risiko ausgewertet, an einer von 34 Arten von Krebs zu erkranken oder zu sterben.

Die Daten wurden unter Berücksichtigung soziodemografischer Faktoren, der körperlichen Aktivität, der Rauchgewohnheiten und des Ernährungsstatus justiert. Der Anstieg des Konsums von UPF um 10% konnte mit einem um 2% erhöhten Risiko, an Krebs zu erkranken, und mit einem 6% erhöhten Risiko, an Krebs zu sterben, in Verbindung gebracht werden.

Zudem wurde festgestellt, dass mit jeder weiteren Konsumerhöhung um 10% das Risiko für Ovarialkrebs um 19% anstieg. Das Risiko, an Ovarialkrebs zu sterben, stieg sogar um 30%. Für Brustkrebs lag dieser Wert bei 16%. Im Vergleich zu den 25% Studienteilnehmenden, die am wenigsten UPF konsumierten, war das Risiko jener 25%, die am meisten UPF konsumierten, bei Krebs allgemein um 7% erhöht, bei Lungenkrebs um 25% und bei Hirntumoren um 52%.

In Bezug auf Kolorektalkarzinome ermittelte eine Studiengruppe bereits 2022 ein um 29% erhöhtes Risiko, wenn Männer hohe Mengen an UPF konsumierten. *(red)*

■

Quelle:

Ewing-Chow D: New Evidence That Ultra-Processed Foods May Increase Cancer Risk. Forbes, 31.01.2023

Literatur:

1 Chang K et al.: Ultra-processed food consumption, cancer risk and cancer mortality: a large-scale prospective analysis within the UK Biobank. eClinicalMedicine 2023; 101840 **2** Wang L et al.: Association of ultra-processed food consumption with colorectal cancer risk among men and women: results from three prospective US cohort studies. Br Med J 2022; 378