ESMO 2022

Review of the European Society for Medical Oncology (ESMO) Congress 2022.

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THREE years after the last in-person European Society for Medical Oncology (ESMO) Congress, the 2022 congress welcomed nearly 23,000 participants in Paris, France, as well as 5,000 online. The purpose of the congress was a celebration of being back together, and of collaboration between all healthcare professionals wanting to improve survival times for patients. During the opening ceremony, Solange Peters, President of ESMO, said: "For ESMO, there was never going to be a return to normal. The only way we know is forward."

In their introduction, Peters highlighted the importance of sustainability in oncology, and how ESMO aims to help achieve this. First, through a qualified medical workforce, by nurturing oncologists' professional development and supporting them in their daily practice. Next, ESMO aims to promote prevention, thereby minimising overall impact of cancer on healthcare resources. Up to half of cancers are deemed preventable. Through adequate prevention and screening initiatives, the absolute number of cases can be lowered and early diagnosis enabled, leading to shorter, less intensive treatment courses. Finally, sustainability can be achieved by caring for the environment in which we operate, contributing to a healthier world. Peters emphasised that the goal is to reduce cancer incidence. It is expected that there will be over 30 million cancer cases worldwide by 2040 (there are currently 19 million). Therefore, sustainability will be critical to ensure the best care possible for patients in the future.

Scientific Co-chairs Charles Swanton and Fabrice André introduced the congress programme, which was constructed to achieve a better understanding of the disease in order to provide better care for patients with cancer, while also caring for sustainability. The focus was on science that impacts patients on a daily basis, rather than virtual science. Major challenges in oncology were integrated in the ESMO programme, including early detection and prevention of cancer; treatment de-escalation thanks to molecular analysis; drugs developed from biotechnologies and impact on infrastructures; molecular medicine to develop new drugs; the impact of new drugs in under-represented populations; and topics needing more attention, such as survivorship and artificial intelligence.

Amanda Psyrri, Chair of the ESMO nomination committee, handed out four awards at the opening ceremony. The first, the ESMO Award, was granted to Karim Fizazi for outstanding contributions to the development of medical oncology, particularly

their contribution to prostate cancer research. Next, Samra Turajlic was awarded the ESMO Award for Translational Research for exceptional achievements in translational research, including their work on cancer evolution, especially in kidney cancer. The third, the Women for Oncology Award, was presented to Fatima Cardoso, for their significant support of the career development of women in oncology, and becoming a role model to a whole generation of women working in oncology. Finally, Bernard Escudier was presented the ESMO Lifetime Achievement Award, for their lifelong commitment to clinical cancer research and education, particularly their achievements in renal cell carcinoma, immunotherapy, and on new therapeutic strategies. During the award ceremony, the recipients from 2020–2021 were also given the opportunity to receive their awards in person.

Peters concluded by saying: "It is also a matter of ensuring that the fruit of the work we do here, our past and future victories in treating cancer more effectively, do not slip permanently out of the reach of patients in the coming year."

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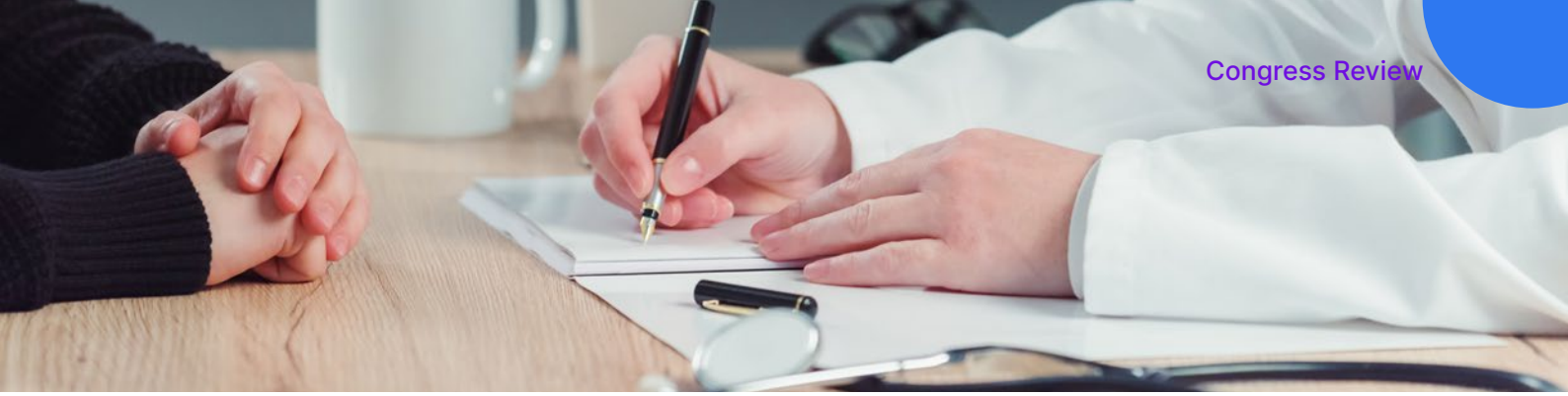
The EMJ team was delighted to attend this event, and is looking forward to attending next year's ESMO congress on the 20th–24th October in Madrid, Spain. Read on for our highlights and reviews of this year's congress. ●



Non-Small-Cell Lung Cancer Could Be Treated with Anti-programmed Death-Ligand 1

ANTI-programmed death-ligand 1 could be used to treat patients with non-small cell lung cancer (NSCLC). A Phase II IPSOS study, which compared single-agent chemotherapy to first-line atezolizumab in patients with NSCLC, was presented at ESMO Congress 2022. It is the first randomised clinical trial to evaluate single-agent immunotherapy in patients with poor prognosis.

The researchers randomised patients with locally advanced or metastatic NSCLC without driver mutations 2:1 to single-agent vinorelbine or gemcitabine in 3/4 weekly cycles, or atezolizumab 1,200 mb intravenously every 3 weeks. The participants were ineligible for first-line platinum-doublet chemotherapy, due to comorbidities in patients aged 70 or over, and due to poor performance status (PS). Atezolizumab improved median overall survival significantly, and these benefits were seen across all subgroups, including PS, histology, and programmed death-ligand 1 expression levels.

This confirms data from the PePS2 trial of pembrolizumab monotherapy in patients with NSCLC and PS of 2, as the median overall survival with atezolizumab is similar. It also confirms that immunotherapy is effective for patients 70 years or over with a PS ≥2 and comorbidities. Lizza Hendriks, Maastricht University Medical Center, the Netherlands, remains cautious, as the question remains of who will benefit from this. They stated: "For relatively stable patients, immunotherapy could be an option, but we must also remain realistic that it will not work for everyone." It is unclear exactly why the patients involved in the trial were not eligible for platinum-doublet chemotherapy. Furthermore, it is unclear what type of patients they were. Hendriks explained that the PS ≥2 can have multiple causes, including the cancer but also comorbidities. This makes it difficult to determine what the optimal management strategy is.

They also said: "It would be interesting to see details of the tumour burden (low tumour burden is often associated with better outcomes with immunotherapy) and comorbidities of patients involved in the trial or how stable they were in terms of PS prior to study enrolment." They concluded that the patients who will benefit from the treatment, as well as biomarkers, need to be identified in order to understand the impact of this study on clinical practice. ●

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Could Sotorasib Improve Progression-free Survival in Pre-treated *KRAS* G12C-mutated Non-small Cell Lung Cancer?

ACCORDING to the results of a Phase III study presented at the ESMO 2022 Congress, sotorasib improves progression-free survival (PFS) compared to docetaxel in pre-treated patients with *KRAS* G12C-mutated non-small cell lung cancer (NSCLC). The study involved patients with *KRAS* G12C-mutated NSCLC that had disease progression following platinum-based chemotherapy and a checkpoint inhibitor. Sotorasib is an oral, irreversible *KRAS* G12C inhibitor, that is approved for the treatment of pre-treated adults with *KRAS* G12C-mutated advanced NSCLC. However, the aim of this study was comparing sotorasib versus docetaxel in KRAS G12C-mutated NSCLC. Comparative studies allow researchers to gain further insight of the disease and therefore accelerate the approval of use in other countries; currently, it has been approved by the U.S. Food and Drug Administration (FDA).

The study participants showed a response of sotorasib versus docetaxel (hazard ratio: 0.66; 95% confidence interval [CI]: 0.51–0.86; p=0.002) after a median follow up of 17.7 months (LBA10). One-year PFS rates were 24.8% for sotorasib and 10.1% for docetaxel and PFS benefit was consistent across subgroups. Furthermore, an objective response rate (ORR) was also remarkably higher with sotorasib (ORR: 28.1%; 95% CI: 21.5–35.4%) than with docetaxel (ORR: 13.2%; 95% CI: 8.6–19.2%; p<0.001); and disease control rate was 82.5% versus 60.3%, respectively.

> **"These results, while supporting a new treatment option, confirm that further improvements are highly sought."**

The study lead, Antonio Passaro from the European Institute of Oncology (IEO), Milan, Italy, stated: "Sotorasib previously received accelerated FDA and conditional [European Medicines Agency] EMA approval in the same setting based on ORR data from the single-arm Phase I/II CodeBreaK 100 trial, but a comparative evaluation was needed to improve the understanding of this molecular-driven disease and move forward the approval in countries where sotorasib is not yet reimbursed."

"These results, while supporting a new treatment option, confirm that further improvements are highly sought after for this specific molecular-driven patient population, and different kinds of combinations are under evaluation in both treatment-naïve and pre-treated settings," Passaro concluded.

Promising New Data Around Antibody–Drug Conjugates

ANTIBODY–drug conjugates (ADC) data shows promise in patients with advanced solid tumours, according to new study data that was presented at the ESMO Congress 2022. The data highlights encouraging safety profiles and responses in individuals with heavily pre-treated malignancies.

Employing a 'Trojan horse' strategy, ADCs use an antibody, which is attached to a chemotherapy agent, that directly targets tumour cells. A Phase I/II dose-finding study of 147 patients with advanced solid tumours unselected for B7-H3 selection received 4.8–16.0 µg/kg of DS-7300. In patients with small-cell lung cancer, 11 out of 19 (58%) had a partial or complete response, with a median duration response of 5.5 months. Further, patients who had received an average of five prior lines had a disease control rate of 71.4% and response rate of 32.0%. While no new safety profiles were reported, more patients in the high-dose cohort had Grade ≥3 treatment-emergent adverse events (TEAE) during a shorter median treatment period than patients on a lower-dose.

The preliminary results of a Phase I dose-escalation and dose-expansion study of zanidatamab zovodotin (ZW49), an ADC, was also presented. Comprised of a bispecific *HER2*-directed antibody and proprietary auristatin toxin, ZW49 was used to treat 77 patients with heavily pre-treated *HER2*-positive cancers (gastro-oesophageal: 27%; breast: 22%). TEAEs were seen in 91% of patients, largely Grade 1 or 2; however, 12% of patients had Grade ≥3 TEAEs. Confirmed objective response rate was 31% and disease control rate was 72% in 29 evaluable patients on ZW49 2.4 µg/kg once every 3 weeks, with two dose-limited toxicities being reported in one patient, which was also observed in one patient on 1.75 µg/kg once a week.

Andrew Furness from the Royal Marsden NHS Foundation Trust, London, UK, and Institute of Cancer Research, London, UK, believes that ADCs show great promise. They noted: "It will be interesting to discover if next-generation ADCs can be developed that are conjugated to treatments other than chemotherapy." ●

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Can Addition of a Tyrosine Kinase Inhibitor Reduce Progression of Renal Cell Carcinoma?

THE COSMIC-313 trial, presented at ESMO Congress 2022, showed that adding cabozantinib, a tyrosine kinase inhibitor, to dual checkpoint inhibitor therapy, significantly prolonged progression-free survival, but increased toxicity. COSMIC-313 is the first trial to show this, and it proves that the triplet regimen can prevent early progression of the disease.

> **"The combination of cabozantinib, nivolumab, and ipilimumab reduced the risk of progression of renal cell carcinoma by 27%, compared with nivolumab and ipilimumab."**

The double-blind, randomised trial included 550 patients with untreated intermediate- or poor-risk advanced renal cell carcinoma. The patients received nivolumab and ipillimumab every 3 weeks for four cycles, then nivolumab every 4 weeks for up to 2 years. The participants were randomised to placebo and cabozantinib according to disease risk and region, and progression-free survival was assessed by blinded independent review. The combination of cabozantinib, nivolumab, and ipilimumab reduced the risk of progression of renal cell carcinoma by 27%, compared with nivolumab and ipilimumab. The objective response rates were 43% for the triplet combination and 36% for the doublet combination.

Viktor Grünwald, University Hospital Essen, Germany, stated we still need to see the overall survival data, and balance the efficacy alongside the toxicity of this new regimen, which shows severe side-effects and toxicity-related treatment discontinuations. Only 41% of patients receiving the doublet combination experienced Grade 3–4 treatment-related adverse events, compared to 73% of patients receiving the triplet combination. Furthermore, 5% of treatment-related adverse events led to discontinuation of all components with the doublet regimen compared to 12% with the triplet. Grade 5 treatment-related adverse events occurred in three patients in both treatment regimens, consisting of gastrointestinal haemorrhage, respiratory failure, and hepatic failure in the triplet regimen; and myocarditis, renal failure, and sudden death in the doublet combination arm. These results mirror those of the CheckMate 9ER trial. More research is needed on the toxicity profile of the triplet regimen to determine its future role. ●

Androgen Deprivation Therapy Beneficial Alongside Radiotherapy in Post-operative Patients with Prostate Cancer

ENCOURAGING results from two Phase III trials (RADICALS-HD and PRESTO), evaluating the use of androgen deprivation therapy (ADT) alongside radiotherapy in post-operative patients with prostate cancer, show metastasis-free and biochemical progression-free survival benefits. This data was presented at ESMO Congress 2022.

The PRESTO trial showed that the primary endpoint, biochemical progression-free survival, was significantly prolonged in patients with high-risk biochemically relapsed prostate cancer after radical prostatectomy, by adding ADT to apalutamide (APA), or to APA and abiraterone acetate plus prednisone (AAP). For ADT+APA, the median biochemical progression-free survival was of 24.9 months, versus 20.3 months for ADT, and 26.0 months for ADT+APA+AAP versus 20.0 months for ADT. Furthermore, the median time to testosterone recovery was 3.9 months for ADT+APA, versus 4.0 months for ADT and 4.8 months for ADT+APA+AAP. The most common Grade ≥2 adverse event, hypertension, was less frequent in the ADT arms (19.4%) than in the ADT+APA (23.4%) and ADT+APA+AAP arm (30.4%).

The RADICALS-HD trial, which studied patients having undergone radical prostatectomy and post-operative radiotherapy showed longer time to salvage ADT, and longer metastasis-free survival (MSF), the primary endpoint, in those who received 24 months versus 6 months of ADT (72% versus 78% at 10 years). While 6 months of ADT improved time to salvage ADT, versus no ADT, it did not improve MFS. Outcomes for MFS with 24 months of ADT versus 6 months, were favourable. The study showed no improvement in overall survival.

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Stephane Supiot, Institut de Cancérologie de l'Ouest and Université de Nantes, France, stated how important these findings are for patients receiving radiotherapy: "The trial results further support the benefit of adding ADT for patients undergoing radiotherapy, but the lack of overall survival benefit of immediate ADT as shown in the DADSPORT meta-analysis (LBA64) can be interpreted that delayed ADT can salvage patients at the metastatic stage." However, they said the findings are not practice-changing yet, as longer follow-up will give more insights into the optimal treatment duration and combinations, as well as toxicity and quality of life.

Results from the First Randomised Study of Peptide Receptor Radionuclide Therapy in Pancreatic Neuroendocrine Tumours

THE FIRST multicentric randomised study to assess the efficacy of peptide receptor radionuclide therapy (PRRT) in patients with advanced pancreatic neuroendocrine tumours has met its primary endpoint.

Presented at the ESMO Congress 2022, results from the OCLURANDOM trial have discovered that progression-free survival (PFS) was longer when patients received the treatment of 177lutetium-octreotate (OCLU) when compared to sunitinib. The study was designed to evaluate the efficacy of PRRT with OCLU in an anti-tumour capacity versus sunitinib, in a cohort of patients with somatostatin receptor scintigraphy-positive unresectable progressive advanced pancreatic NETs.

The patient group of 84 individuals included those who had been previously treated with Eastern Cooperative Oncology Group (ECOG) Performance Status 0–2, and who had documented disease progression within the year prior to the beginning of the study. Patients had a mean age of 63 years, and 52% were female. Forty-two percent had >25% liver involvement; 37% had Ki-67 >10%; 20% had functioning syndrome; and 43% had received two or more lines of systemic therapy. Forty-four percent of patients experienced Grade 3–4 adverse events in the OCLU arm compared to 63% in the sunitinib arm (decreased blood cell count: 12% versus 23%; digestive problems: 12% versus 21%; hypertension: 12% versus 19%; fatigue: 7% versus 12%).

These patients were randomised 1:1 to receive either OCLU (4.0×7.4 GBq infusions every 8 weeks), or sunitinib (37.5 mg per day). Based on a Fleming design hypothesis, the primary endpoint was if 19 or more patients had no disease progression or had not died after the initial 12 months, OCLU was considered an effective treatment for advanced pancreatic NETs.

The study met this primary endpoint, with significantly longer PFS in those patients receiving PRRT with OCLU versus sunitinib. Twelve-month PFS rates with OCLU were 80.5% (33/41 patients; 90% confidence interval [CI]: 67.5–89.9) versus 42% of patients with sunitinib (18/43 patients; 90% CI: 29.1–55.5). Median PFS for OCLU was 20.7 months (90% CI: 17.2–23.7), versus 11.0 months (90% CI: 8.8–12.4) with sunitinib.

Irene Burger, Kantonsspital Baden, Switzerland, commented that the study "fills an important gap, despite some limitations such as the heterogeneity of prior therapeutic regimens." ●

"The study met this primary endpoint, with significantly longer PFS in those patients receiving PRRT with OCLU versus sunitinib."