Congress Review

Review of the European Society for Medical Oncology (ESMO) Congress 2021: An Enhanced Virtual Experience

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AN INTERNATIONAL COLLECTIVE of oncology clinicians and researchers came together to share the most recent updates in patient care and research at the European Society for Medical Oncology (ESMO) Congress 2021. Considering the current climate, ESMO 2021 was designed as an enhanced virtual experience, allowing more than 23,000 to attend from their homes, with an audience of 300 in-person in Paris, France. The mixed virtual format allowed the advancements, networking opportunities, and collective understanding of oncological care to be communicated to audience members around the world whilst maintaining the traditional congress atmosphere. ESMO President, Solange Peters, described this year's congress as "the place where oncology experts come together, as a community."

The opening session was chaired by Peters who used her time to introduce the launch of ESMO's new initiative the International Cancer Foundation (ICF). By 2040 cancer incidence could rise to almost 30 million cases, with the largest increase seen in low- and middle-income countries. The ICF aims to bring cancer care across borders, spreading effective diagnosis, treatment, cure, and follow-up care. The ICF is the embodiment of what cancer care means to ESMO, supporting doctors everywhere and expanding the organisations reach to regions where optimal cancer care might currently seem unimaginable. Peters explained that the ICF would focus on prevention, patient resources and the provision of new fellowships, all supported by the full weight of the ESMO communities' expertise in oncology and cancer care.

The ESMO 2021 Congress featured 1,989 abstracts as well as 68 that were classed as late breaking abstracts. Several of these abstract authors provided summaries of their research that are included in this issue of *EMJ Oncology*.

"The mixed virtual format allowed the advancements, networking opportunities, and collective understanding of oncological care to be communicated to audience members around the world whilst maintaining the traditional congress atmosphere."

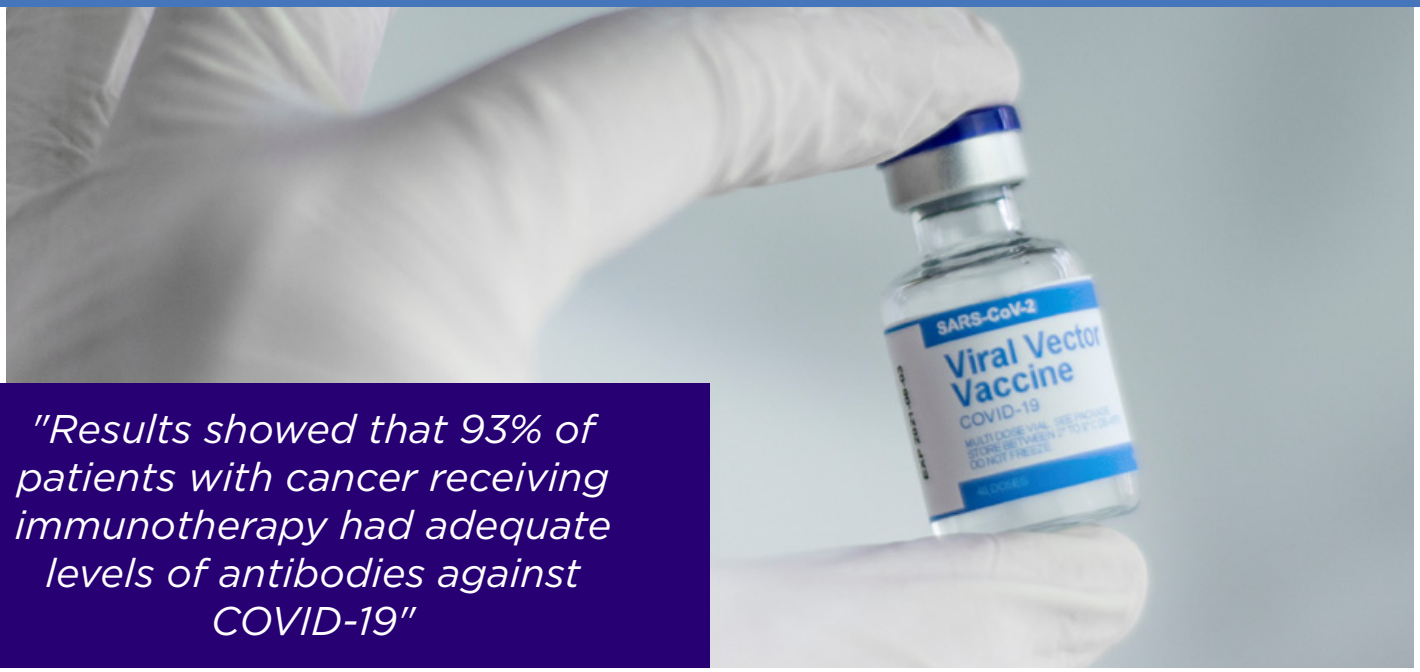
The featured abstracts range from an analysis of the efficacy of COVID-19 vaccines in patients with cancer to repurposing cancer drugs to prolong survival in prostate cancer patients to a more holistic analysis of the frequent exclusion of children from their parent's cancer journey.

The five-day congress featured more than 450 speakers, with almost 200 hours of content and 17 special sessions. Pasi Jänne, Scientific Co-chair, ESMO Congress 2021, gave an overview of some of the standout highlights that were showcased over the long weekend. Presidential symposia, presented on Saturday, included a session communicating updates in metastatic breast carcinoma as well as the outcome of adjuvant studies in melanoma. This was followed on Monday by a presidential symposium that spotlighted the rare malignancy pheochromocytoma and paragangliomas. A novel type of session introduced at ESMO 2021 were the controversy sessions. These explored wide ranging topics from molecular profiling in patients with colorectal cancer to the validity of patient derived cancer models in clinical decision making. These were topics that currently provide some degree of controversy in how to best manage patients and the sessions were interactive, allowing the audience both at home and in-person to hear differing points of view and express their own opinions.

The research and achievements of a wide range of clinicians and researchers were highlighted over the course of the congress. However, a particular mention must be given to the winners of the four ESMO awards. These were awarded on behalf of the ESMO community, and the winners were determined by the ESMO Nominating Committee and ESMO Council. The ESMO Award was presented to Lisa Licitra, Interim Director of Medical Oncology, Head and Neck Cancer Department, Instituto Nazionale Tumori, Milan, Italy. The ESMO Award for Translational Research is presented to candidates who are internationally recognised for their outstanding achievements. This year's commendation was awarded to George Coukos, Ludwig Institute for Cancer Research, Lausanne University Hospital, Lausanne, Switzerland. Rebecca Dent, Department of Medical Oncology, National Cancer Centre, Singapore, won the ESMO Women for Oncology Award and Alex A. Adjei, Mayo Clinic, Rochester, Minnesota, USA won the ESMO Lifetime Achievement Award for his work in drug development, focusing on evaluating mechanisms of drug action and synergistic drug combinations.

The ESMO Congress 2021 demonstrated the first steps towards moving back to in-person, traditional medical congresses in the wake of the last 18 months. EMJ looks forward to hopefully welcoming you all in-person next year at the 2022 ESMO Congress in Paris. However, until then, read on for the latest in key scientific insights from ESMO Congress 2021.

ESMO 2021 REVIEWED →



"Results showed that 93% of patients with cancer receiving immunotherapy had adequate levels of antibodies against COVID-19"

COVID Vaccines Successfully Protect Patients with Cancer

UNTIL recently, there was a lack of research as to whether COVID-19 vaccines were effective in patients with cancer. However, new research presented at this year's ESMO Congress revealed how patients with cancer have a suitable response to the vaccine and studies suggest that a third booster vaccine could further improve immunisation against COVID-19.

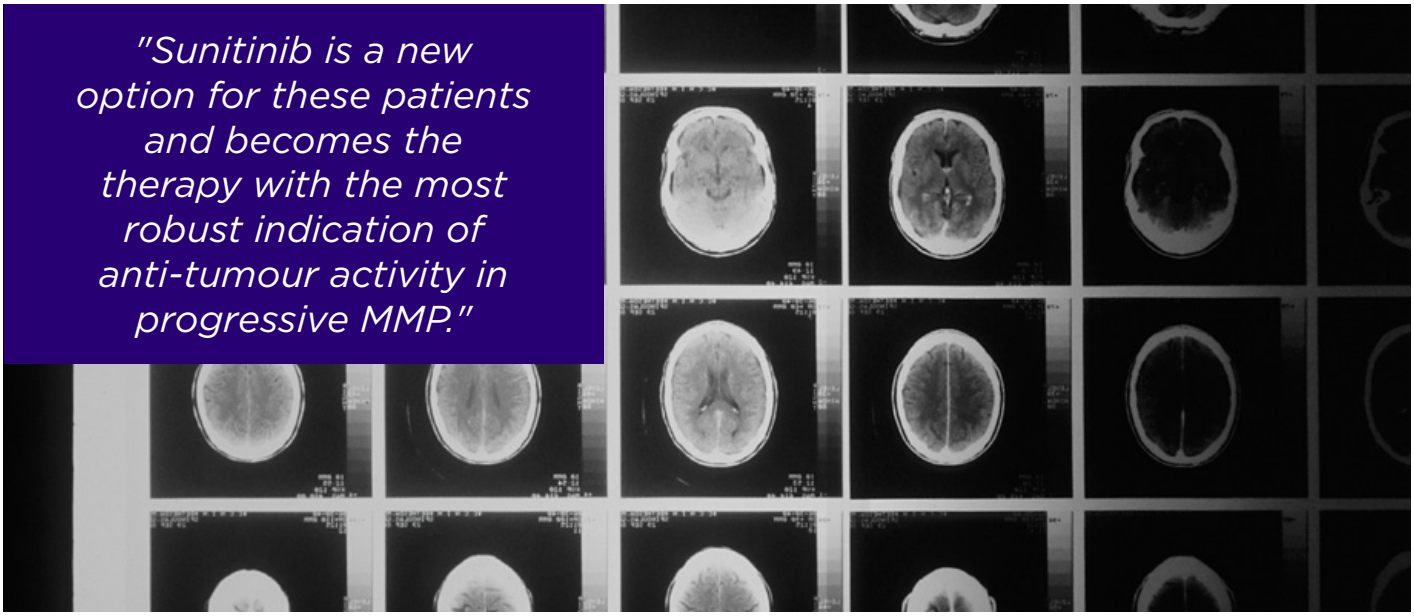
One notable study, namely VOICE, explored whether different oncological treatments affected vaccination against COVID-19. The study recruited almost 800 patients from numerous hospitals from the Netherlands. The patients were split into four groups: patients with cancer treated with immunotherapy, patients with cancer treated with chemotherapy, patients with cancer treated with a combination of chemo- and immunotherapy, and, finally, individuals without cancer.

The antibody levels of the individuals were measured after 28 days after the second dose of the Moderna (Mrna-1273) vaccine. Results showed that 93% of patients with cancer receiving immunotherapy had adequate levels of antibodies against COVID-19. Similarly, 84% of patients receiving chemotherapy and 89% of patients receiving chemo-immunotherapy had adequate levels of antibodies. To summarise, patients are sufficiently protected regardless of their oncological treatment. Comparing these results to individuals without cancer shows that antibody levels are almost just as high after two doses.

Fascinatingly, results from another study showed that patients with cancer who had two doses of AstraZeneca's COVID-19 vaccine or tozinameran and had previously contracted COVID-19 had higher levels of antibodies against COVID-19, including against the deadlier Delta variant. These results highlight the importance of patients having two doses against COVID-19 and even suggest that a booster shot could increase efficacy for more patients.

The president of ESMO, Solange Peters, concluded: "Since the very start of the pandemic outbreak, we at ESMO have made it a top priority to secure extra care for our patients: first by educating oncology colleagues throughout these unprecedented events, then by pushing for the prioritisation of COVID-19 vaccination for patients with cancer." The promising results from these studies presented at the ESMO congress prove that the COVID-19 vaccination is just as safe for patients with cancer as it is for healthy individuals. ■

"Sunitinib is a new option for these patients and becomes the therapy with the most robust indication of anti-tumour activity in progressive MMP."



Tyrosine Kinase Inhibitor as Practice Changing New Medication for Rare Neuroendocrine Tumours

PROGRESSION-FREE SURVIVAL (PFS) in malignant pheochromocytoma and paraganglioma (MPP) is prolonged by more than 5 months by sunitinib, a recent randomised trial has found. These break through results from the FIRSTMAPPP trial were presented at the ESMO Congress 2021, which was held in Paris and virtually from the 16th–21st of September.

MPP is a very rare form of neuroendocrine tumour. Annual incidence is less than 1 per million. FIRSTMAPP enrolled 78 patients with progressive MPP over an 8-year period from 15 centres across Europe. Patients were randomly allocated to sunitinib or placebo.

The primary endpoint for the study was PFS at 12 months. This was achieved by 35.9% of the sunitinib group (n=14) compared with 18.9% in the placebo group. The median PFS was 8.9 months versus 3.6 months in the sunitinib and placebo groups, respectively.

"None of the treatment options we currently have for advanced MPP are supported by randomised clinical trial evidence. This disease is commonly treated using combined chemotherapy with cyclophosphamide, vincristine and dacarbazine, all quite old agents and all very toxic. Sunitinib will be much better tolerated," commented Juan Valle, Consultant Medical Oncologist, University of Manchester and the Christie NHS Foundation Trust, Manchester, UK.

Throughout the trial, severe adverse events occurred in 54% of patients in the sunitinib group compared with 49% in the placebo group. The most frequent adverse events were asthaenia/fatigue (18% versus 3%) and hypertension (10% versus 6%). There was 1 death in both arms of the study.

"The study demonstrates that sunitinib 37.5 mg per day was tolerable," explained Eric Baudin, Chair, Neuro-Endocrine Tumours, Gustave Roussy – Cancer Campus, Villejuif, France. "In particular, we know that two-thirds of patients with MPP have hypertension due to high levels of hormones, yet hypertension induced by the drug was manageable."

Baudin further highlighted the value of the research: "This trial provides the highest level of evidence ever reached in this very rare cancer. The results are practice changing. Sunitinib is a new option for these patients and becomes the therapy with the most robust indication of anti-tumour activity in progressive MPP." ■

CDK 4/6 Inhibitors Show Prolonged Survival for Metastatic Breast Cancer

"To put these results into perspective, in my 45 years as an oncologist there have been tens of thousands of clinical trials for breast cancer and while a PFS benefit has been shown many, many times, we have rarely observed an improvement in overall survival"

BREAKING research has found that the administration of a CDK 4/6 inhibitor alongside first-line hormonal treatment in postmenopausal woman with hormone receptor positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer improves survival rates by 1 year. This evidence comes from the MONALEESA-2 trial, and was presented on 19th September at the ESMO Congress 2021.

The randomised trial, which is the first to bring a statistically significant survival outcome in this patient demographic, involved 668 patients who had not previously received endocrine therapy, chemotherapy, or a CDK 4/6 inhibitor. The trial focused on progression free survival. Individuals were administered a combination of either ribociclib (a CDK 4/6 inhibitor) plus letrozole, and aromatase inhibitor, or a placebo plus letrozole. The trial measured overall survival after 400 deaths, and saw the active treatment plus letrozole with a median rate of 63.9 months, and the placebo group with a median overall survival of 51.4 months. "To put these results into perspective, in my 45 years as an oncologist there have been tens of thousands of clinical trials for breast cancer and while a progression free survival benefit has been shown many, many times, we have rarely observed an improvement in overall survival," explained Gabriel Hortobagyi, Professor of Medicine, Department of Breast Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, USA.

"It is important to note that these data are related to endocrine-sensitive patients who had not previously received endocrine therapy for metastatic disease. The clinical implication is that now we have a clear demonstration that the combination of endocrine therapy plus the CDK 4/6 inhibitor ribociclib prolongs both progression free survival and overall survival," noted Giuseppe Curigliano, Clinical Director, Division of Early Drug Development for Innovative Therapy, European Institute of Oncology, Milan, Italy. He went on to highlight that further research could present the opportunity to detect biological features to identify individuals that would benefit from this treatment the most; research with this focus currently ongoing, carried out by Hortobagyi and colleagues.

Hortobagyi concluded the study by highlighting that the results obtained from this trial can be extrapolated to patients with hormone receptor positive, HER2-negative metastatic breast cancer from around the world, providing further benefit to the study. "While this is the only CDK 4/6 inhibitor to demonstrate an overall survival benefit in this patient population so far, we are still waiting for results of the palbociclib and abemaciclib trials. And of course, there are other emerging treatments such as other kinase inhibitors so there is more research to come in this field," he added, hinting at the future research that we can expect to see in this area of oncology. ■

Could Drug Repurposing Prolong Survival in Prostate Cancer Patients?

EMERGING research has suggested that a unique combination of existing drugs is able to improve survival rates in patients with hormone/castration-sensitive prostate cancer. Presented at the ESMO Congress 2021, this evidence comes from the PEACE-1 and STAMPEDE studies, which both revealed that the administration of standard therapy alongside abiraterone acetate plus prednisolone (AAP) prolonged patient survival compared to standard therapy alone.

"The administration of AAP alongside docetaxel and ADT saw a 25% reduction in mortality risk compared to docetaxel and ADT, as well as 2.5 years of progression free survival in men with high-burden metastatic prostate cancer."

For patients with metastatic prostate cancer, the standard treatment for decades was androgen deprivation therapy (ADT). Recently, docetaxel, a drug used in chemotherapy and the hormonal agent abiraterone were both found to prolong survival when administered alongside ADT. The PEACE-1 trial compared the clinical benefits of using different combinations of these drugs alongside ADT, and found that a combination of three drugs both prevented cancer progression, and improved patient survival. The administration of AAP alongside docetaxel and ADT saw a 25% reduction in mortality risk compared with docetaxel and ADT, as well as 2.5 years

of progression-free survival in men with high-burden metastatic prostate cancer.

"PEACE-1 is the first trial to establish that triplet treatment should be offered to these men, especially those with the most aggressive cancers (those with multiple metastases)" stated Karim Fizazi, Medical Oncologist, Institute Gustave Roussy and Professor in Oncology, University of Paris-Saclay, France. He also noted that the side effects experienced following this treatment were mild, with few severe side effects occurring. Fizazi went on to emphasise that although systemic triplet treatment halts cancer progression, a follow-up is needed to assess survival in patients with low-burden metastatic prostate cancer.

The STAMPEDE trial, which focused on non-metastatic prostate cancer with a high-risk of spread, saw an improvement in overall survival rates following administration of standard treatment of ADT alongside AAP for 2 years. With this treatment, metastasis-free survival increased from 69% to 82%, overall survival increased from 77% to 86%, and prostate cancer-specific survival improved from 85% to 93%. Gerhardt Attard, John Black Charitable Foundation Endowed Chair in Urological Cancer Research at University College London, UK, explained: "Based on these results, all men with high-risk non-metastatic prostate cancer should be considered for 2 years of abiraterone. This will involve more hospital visits during this period to manage administration of the drug but by reducing subsequent relapse, may reduce the overall burden for both patients and health services."

Although positive results were also seen in the STAMPEDE trial, Attard also added that further trials need to be carried out to optimise the length of AAP therapy, a factor which was not studied in the trial. Maria De Santis, Chair of Interdisciplinary Urological Oncology, Department of Urology, Charité Universitätsmedizin, Berlin, Germany, explained: "With regards to the non-metastatic patients in STAMPEDE, this is a completely new patient group that has not been included in other published trials. The addition of systemic treatment with AAP for at least 2 years in this population will change our former treatment strategy, which has been only ADT plus or minus radiotherapy to the prostate for many years."

The benefits of repurposing these pre-existing drugs alongside standard therapy are clear, particularly given that drug approval is not required, allowing for quicker implementation into clinical practice. Future studies will likely focus on adjusting the combination of each therapy as well as treatment length in hope to optimise patient survival. ■

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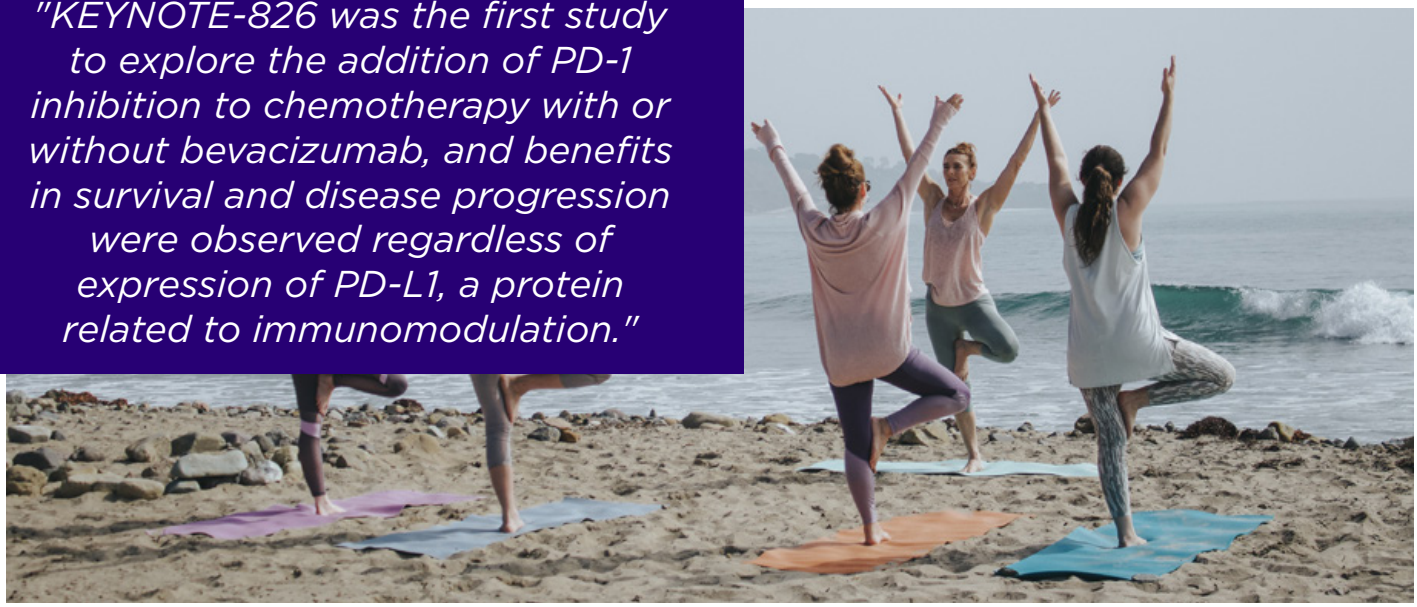

Survival of Patients with Persistent, Recurrent, or Metastatic Cervical Cancer Could Be Prolonged by Immunotherapy

ACCORDING to a study, presented at the ESMO Congress on 18th September 2021, additional immunotherapy to standard first-line treatment prolongs survival by 8 months in patients with persistent, recurrent, or metastatic cervical cancer.

Cervical cancer is the second most common cancer in females aged 15–40 years, with roughly 340,000 deaths documented in 2020. The KEYNOTE-826 trial randomly assigned 617 females to either immunotherapy (pembrolizumab) or placebo. Additionally, the two groups also underwent chemotherapy (paclitaxel plus the doctor's choice of carboplatin or cisplatin) and, at the doctor's discretion, they could also receive bevacizumab. According to the results, the addition of pembrolizumab reduced the death risk by 33% and further lowered the disease progression or death by 35%. Anaemia was the most commonly observed side effect with 30.3% in the pembrolizumab group and 26.9% in the placebo group. Secondly, a lower concentration of white blood cells was noted at 12.4% in the pembrolizumab group compared with 9.7% in the placebo group. However, the observed side effects were manageable and expected based on previous study. Bevacizumab was administered to 63% of the participants and the authors confirmed that this drug should only be used with the pembrolizumab when safe. However, there was still a clinical benefit in the addition pembrolizumab to chemotherapy alone. Unfortunately, one of the study limitations was that it was not designed to statistically compare the outcomes as the administration of bevacizumab was not randomised.

One of the study authors, Nicoletta Colombo, Director of the Gynaecology Programme, European Institute of Oncology, Milan, Italy, said: "Previous studies showed that adding anti-angiogenesis therapy with bevacizumab to chemotherapy prolonged survival by 3.7 months over chemotherapy alone. KEYNOTE-826 was the first study to explore the addition of PD-1 [programmed cell death protein-1] inhibition to chemotherapy with or without bevacizumab, and benefits in survival and disease progression were observed regardless of expression of PD-L1 [programmed death-ligand 1], a protein related to immunomodulation. Side-effects with the new combination therapy were manageable and the observed adverse events were as expected based on previous data on the individual drugs." ■

Recurrence of Stage IIB and IIC Melanoma Could be Reduced by Adjuvant Immunotherapy

ACCORDING to the first Phase III randomised clinical trial, presented at the ESMO Congress on 18th September 2021, Stage II melanoma reoccurrence could be reduced by 35% by using adjuvant pembrolizumab. Patients with Stage IIB and IIC melanoma and those diagnosed with Stage IIIA and IIB melanoma have the similar risk rate of disease reoccurrence and death. A deep or ulcerated tumour is observed in patients with Stage IIB and IIC melanoma. Regardless of the similar risks associated, with both Stage IIB and IIC melanoma and Stage IIIA and IIB, currently only Stage IIIA and IIB standard of care is adjuvant immunotherapy.

The novel KEYNOTE-716 study, for a period of up to 1 year, randomly assigned 976 patients with complete resection of cutaneous Stage IIB or IIC melanoma and no lymph node involvement to either programmed cell death protein-1 (PD-1) inhibitor pembrolizumab or a placebo. Within a median follow up period of 14.4 months, the results showed that reoccurrence was observed patients on pembrolizumab 54 (11.1%) compared with 82 (16.8%) patients on placebo. Furthermore, the distance reoccurrence was nearly halved with pembrolizumab compared with the placebo (23 and 38 events, respectively). Additionally, this study was not just centred to adults but also adolescents and children over 12 years old.

Study author Jason J Luke, Director of the Cancer Immunotherapeutics Center, University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center, USA stated that "there has been a belief that early-stage melanoma doesn't recur very fast and that these patients don't develop metastatic disease. These data clearly disprove that and show that patients with high-risk Stage II melanoma recur quickly and distantly, just the same as patients with Stage IIIA and IIIB. Treatment with pembrolizumab reduced that in a meaningful and statistically significant way, indicating that these Stage II patients should be offered adjuvant therapy." This study could be beneficial, with the potential to reducing recurrences and metastases in patients diagnosed with Stage IIB and IIC melanoma and could be used as a benchmark in associated future studies. ■

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Insufficient Follow-Up Care for Cancer Survivors

RECENT evidence has emerged from the ESMO 2021 Congress suggesting a disparity between standards of cancer follow-up care and current patient needs following treatment. This information was presented on 18th September 2021 and is thought to have stemmed from the significant improvements in cancer screening and treatment leading to earlier diagnosis, all of which contribute to long-term survival rates. A study presented alongside this research confirmed this discontent amongst the population of cancer patients.

Over half of patients in Europe now beat cancer and experience long-term survival rates of over 5 years following diagnosis, a statistic that should be positive for survivors. However, the residual impact of the disease coupled with side-effects of anticancer medicines sees a significant proportion of patients continuing to suffer from hampering symptoms, which, unfortunately, impedes a smooth return to normal life. Dorothy Keefe, CEO of Australia's National Cancer Agency, Cancer Australia, Sunny Hills, Australia, and Chair of the ESMO Supportive and Palliative Care Track, explained: "This is probably due to the increase in survival rates itself lagging behind the introduction of new therapies, but also to a lack of prioritisation compared to the need to develop a cure."

Both patients and survivors commonly experience cancer-related fatigue, which is described as a persistent sense of exhaustion that is not alleviated by sleep or rest and that interferes significantly with the person's usual functioning. The FiX study aimed to assess the patterns, severity, and management of cancer-related fatigue in 2,508 patients with 15 different cancer types. Forty percent of

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participants reported a moderate-to-severe burden from continued fatigue 4 years post-diagnosis in a follow-up survey conducted alongside the study. Over 40% of patients additionally experienced loss of physical ability, whilst over 30% reported sleeping problems, sexual problems, joint pain, and anxiety, all of which caused moderate burden.

"Despite increasing awareness of the effectiveness of mitigating measures like exercise to reduce fatigue, patients are still too often left alone to seek help for symptoms that cannot be directly addressed with medicines in the same way as something like pain, for which satisfaction with the support received was high in our study," noted study author Martina Schmidt, German Cancer Research Centre (DKFZ), Heidelberg, Germany. Schmidt went on to highlight the importance of long-term follow-up care involving additional systematic screening to identify these burdens and relieve patients of these symptoms as early as possible, as well as ensuring that individuals are well-informed of potential symptoms.

Keefe added: "This research shows that a staggeringly high number of patients still suffer from significant health issues years after being declared disease-free. Their dissatisfaction with the care available is a wake-up call that we should be paying more attention to these individuals, trying to understand the mechanisms at play in order to identify interventions that could help them to better recover." Currently, methods of managing these adverse symptoms are untested, warranting the implementation of a survivorship plan for patients. Keefe further explained: "Going forward, we need to develop these models of care in a way that minimises the burden on healthcare systems, implement them and research their impact so that we can come back in five years' time and evaluate whether they have made a difference for cancer survivors." ■

Is the Pace of Oncology Advancements Leaving Doctors and Patients Behind?

BREAKING RESEARCH has highlighted the growing difficulty experienced by both doctors and patients attempting to keep up with the rapid pace of developments within the field of oncology, particularly those brought on by cancer immunotherapy. Two studies presented at the ESMO Congress 2021 suggested that doctors who are not specialists in oncology struggled to keep up with the evolution of prognosis and had limited knowledge of available medicines and their potential side effects. Both studies emphasised the need for broader education on current standards of care.

CareAcross, a multilingual platform providing personalised education for cancer patients, conducted a survey amongst 5,589 of its members to evaluate patients' knowledge about immunotherapy. "It is essential for these individuals to be well-informed because it is a complex treatment that is too often mistaken for a miracle cure," stated Paris Kosmidis, Chief Medical Officer, CareAcross, and study author. Patients were asked several questions regarding immunotherapies mechanism of action, efficacy, side effects and cost.

Almost half of participants diagnosed with either breast, lung, prostate, or colorectal cancer answered that they were unsure or did not know how immunotherapy worked, with only 32% selecting the correct answer, "activates the immune system to kill cancer cells".

Understanding how cancer care has evolved is also essential for medical professionals outside of oncology. Conleth Murphy, Bon Secours Hospital Cork, Ireland, author of the second study conducted a survey exploring physicians' perceptions of cancer prognosis. This survey asked 301 non-oncology physicians and 46 medical and radiation oncologists to estimate patients' 5-year survival rates for 12 of the most common tumour types across all stages of disease. Their answers were then compared with the most recent survival figures from the National Cancer Registry of Ireland.

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The non-oncologists were able to provide accurate estimates of all-stage survival for only 2 out of the 12 cancer types. When they were provided with specific clinical scenarios, non-specialists significantly underestimated 5-year survival and tended, overall, to be more pessimistic than oncologists. To avoid presenting patients with unduly bleak expectations, Murphy recommended that non-oncologists should always refrain from answering patients' questions with numbers.

"Amid this growing complexity, an important part of the family doctor's role in a patients' journey with cancer is reformulating information they have been given by their oncologist to give them a better understanding of their situation," stated Cyril Bonin, General Practitioner, Usson-du-Poitou, France. "More consistent communication with the oncology team about the therapy's expected benefits, possible side-effects and impact on prognosis could help us guide patients competently and provide the psychological support they need." ■

Children Often Excluded from Their Parent's Cancer Journey

IGNORANCE is not bliss for children of patients with cancer, according to new research presented at the ESMO Congress on 16th September 2021. Last year, an estimated 4.6 million individuals aged 20–54 were diagnosed with cancer. These are the ages when people are most likely to be raising children, meaning many children would have also been affected by these diagnoses.

A novel study, surveying 103 patients with cancer in Tunisia, reported that nearly 90% of patients struggled to communicate about their disease with their children, while 40% chose not to reveal the whole truth. Study author Sinen Korbi, Institute Salah Azaiez, Tunis, Tunisia, stated that this resulted from parents wanting to protect their children. However, 96% of patients saw behavioural changes such as anxiety and depression in their children, which affected academic life and even led to substance abuse in some.

Communication about cancer with children is an ongoing process. Parents should ask how their children are doing and explain their disease in an age-appropriate way. Although he was not involved with the study, clinical and child psychology expert Carlo Alfredo Clerici, University of Milan, Italy, believes that a certain amount of knowledge about their parent's disease can protect children from traumatic phenomena. However, this new study reported that many parents needed guidance on how to broach this topic.

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While this study highlights parent's struggle to communicate about their disease with their children, Clerici stated: "Future research should also aim to capture traumatic phenomena that unfold over time, and which are associated with more worrying long-term consequences than the individual symptoms of distress reported here." ■