COLAB.NOTEBOOK

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notes highlights from the ASCO 20 virtual scientific meeting - including new updates in practice changes and standards of care across tumour sites

UNITE AND CONQUER. ACCELERATING PROGRESS TOGETHER ASCO 2020

thousands of oncology professionals from around the world gathered virtually for ASCO 2020 to hear the latest research in the treatment and care of people with cancer. ASCO, a highlight in the cancer research calendar. ASCO receives some 40,000 participants at McCormick centre in chicago, which held online due to the ongoing CO VID 19 pandemic. McCormick centre itself was transformed into a field hospital to deal with the city's COVID 19 crisis.

everything is different this year, but innovation must continue, change is inevitable, and collaboration is key - there are certainly many lessons we can learn from this ongoing pandemic, especially as we look forward to cancer care. to ensure we continue to meet the needs of cancer patients in canada and globally, we must continue to collaborate to ensure not only the exchange of knowledge, as this report is meant to do, but also that together we can make a bigger impact to change cancer.

CANCER AND COVID 19

the ASCO20 virtual scientific program featured a special session examining the impact of COVID-19 on people with cancer. COVID-19 caused by the novel coronavirus [SARS-CoV-2] has had a significant impact on global health. two studies in this special session highlighted show how the oncology community is actively working together to learn more about how this disease and how it is affecting people with cancer. these analyses are based on data collected over two months, with both studies beginning in early march as COVID 19 became more widespread within europe and north america.

WHILE RESEARCHERS CONTINUE TO HAVE MORE QUESTIONS, THESE FINDINGS HELP PROVIDE INSIGHTS INTO OUTCOMES FOR PATIENTS WITH CANCER WHO DEVELOP COVID-19 THIS IS EARLY RESEARCH AND MUCH MORE STILL NEEDS TO BE LEARNED

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access to care, access to clinical trials, and access to information is really key.

we are strongest together.

we are united in our mission to reduce the global burden of cancer.

HOWARD ‘SKIP’ BURRIS
outgoing ASCO president

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CANCER AND COVID 19

clinical impact of COVID 19 on patients with cancer. data from the COVID 19 and cancer consortium [CCC19] abstract LBA110

the COVID 19 and cancer consortium is designed for healthcare professionals to report patients whom they are treating for cancer and have also tested positive for COVID 19, in an effort to collect data and distribute information about this specific patient population. in april 2020, the multi centre effort gained international members–making it a worldwide collaboration. early data from the registry was presented as part of a late breaking abstract.

an analysis of data from 928 people with cancer and COVID-19 has found that having active, progressing cancer was associated with an increased risk of death. other factors strongly linked with increased death include treatment for COVID 19 with hydroxychloroquine and azithromycin, being older than 70 years, and a reduced ability to perform daily tasks.

other factors that were less strongly associated with an increased risk of dying among older patients - the risk of dying further increased by nearly two times for every decade of life.

having stable, non progressing cancer was associated with a 1.79 times greater risk of dying than having no evidence of disease. men had a 1.63 times greater risk of dying in 30 days than women. having smoked regularly in the past was linked to a 1.6 times greater risk of dying than having never smoked.

half of the patients in this study are white, 16% black, 16% hispanic, and 15% other races and ethnicities. the most common types of cancer in this group were breast cancer [21%], prostate cancer [16%], gastrointestinal cancers [12%], lymphoma [11%], and thoracic cancers [10%]. among these patients, 43% had active, or measurable, cancer, 39% were in active cancer treatment, and 45% were in cancer remission.

in this study, 121 patients died within 30 days of the COVID 19 diagnosis. researchers found that people with cancer that was actively progressing, were 5.2 times more likely to die within 30 days than people with cancer in remission or with no evidence of disease [NED].

the patients' ability to perform daily tasks was measured with the ECOG performance status score. a performance status score of 2 or more was linked with a nearly four times greater risk of death within 30 days than in those who had a performance status score of 0 or 1.

researchers also found that COVID 19 treatment with a combination of hydroxychloroquine and azithromycin increased the risk of dying by nearly three [3] times, compared with those who did not receive these drugs. no significant increase in the risk of dying was found if a patient received either of these drugs separately. those who received the combination of hydroxychloroquine and azithromycin and died were also more likely to have a performance status score of 1, have received cancer treatment less than two weeks before the COVID 19 diagnosis, have a positive blood type, have a non hispanic ethnicity, and have previously received statins to treat cholesterol.

across all patients in this analysis, 466 [50%] were hospitalized due to illness and 132 [14%] needed to be admitted to the intensive care unit [ICU]. a total of 116 patients [12%] had to be put on a ventilator, and 405 patients [44%] needed additional oxygen.

conclusions - all cause 30 day mortality and severe illness in this cohort were significantly higher than previously reported for the general population and were associated with general risk factors as well as those unique to patients with cancer. cancer type and treatment were not independently associated with increased 30 day mortality. longer follow up is needed to better understand the impact of COVID19 on outcomes in patients with cancer, including the ability to continue specific cancer treatments.

what does this mean - the impact of COVID 19 infection on cancer management and outcomes must be evaluated. researchers are working to quickly get information about why some patients with cancer become infected with SARS-CoV-2 virus and identify the factors that affect disease severity and death. they are also interested in the effects of treatments that are being used to treat patients with cancer who have COVID-19.

THIS KNOWLEDGE CAN HELP GUIDE THE MEDICAL RECOMMENDATIONS FOR PEOPLE WITH CANCER DURING THIS GLOBAL PANDEMIC.

previous chemotherapy is linked with increased risk of death in people with thoracic cancer and COVID-19 abstract LBA111

analysis from the TERAVOLT registry suggests that chemo within three months of a COVID 19 diagnosis lead to higher risk of death for patients with thoracic cancers

a global consortium to collect data on patients with thoracic malignancies diagnosed with COVID 19 infection to understand the impact on this patient population. goals of this consortium are to provide data for guidance to oncology professionals on treating patients with thoracic malignancies while understanding the risk factors for morbidity and mortality from this novel virus.

researchers found that patients receiving chemotherapy [CT] within the last three months had a 64% higher risk of dying from COVID 19. at the time of this analysis, 144 patients had died. of those, 112 [79.4%] died from COVID 19 and 15 [10.6%] died from cancer. among those who died were 66 patients [46.8%] receiving CT, 18 patients [12.9%] receiving tyrosine kinase inhibitors [TKI], and 22 patients [31.0%] receiving immunotherapy [ICI] alone or in combination with CT. the increased risk from CT remained whether the treatment was given alone or in combination with other therapies. treatment before a COVID 19 diagnosis with corticosteroids was also linked to an increased risk of 1.5 times higher risk of death in people with thoracic cancer than in those who did not take them. researchers also saw a possible connection between earlier treatment with anticoagulants and increased risk of death, but there were too few patients who took them in the study to further investigate this observation. the type of treatment given for COVID 19 did not appear to affect a patient's risk of dying. .

PRE EXISTING LUNG DAMAGE, SMOKING STATUS, ADVANCED AGE AND CO-MORBIDITIES MAKE THORACIC CANCER PTS MORE VULNERABLE TO COVID 19

conclusions- in patients with thoracic malignancies who develop COVID 19, baseline risk factors for mortality included age, performance status and presence of comorbidities. no impact of gender, BMI, smoking status, stage or type of cancer was observed for risk of death. patients on steroids or anti coagulates prior to diagnosis are ar increased risk of mortality. prior administration of chemotherapy as a unique modality or in combination with immune checkpoint inhibition [ICI] is associated with an increased risk of death while ICI and TKI therapy are not. therapy administered to treat COVID 19 is not significantly associated with outcomes.

what does this mean- this study provides scientific evidence that for people with thoracic cancers and COVID-19, chemotherapy within three months of a COVID-19 diagnosis, as well as treatment with corticosteroids before COVID 19, increases the risk of dying.

THIS KNOWLEDGE CAN HELP SUPPORT THE DEVELOPMENT OF MORE DETAILED MEDICAL GUIDANCE ABOUT HOW BEST TO CARE FOR PEOPLE WITH THORACIC CANCER DURING THE COVID-19 PANDEMIC.

RESEARCH MAKING A DIFFERENCE IN PATIENT CARE

pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer. the phase 3 KEYNOTE-177 study abstract LBA4

pembrolizumab increases progression free survival in MSI-H/dMMR metastatic colorectal cancer twice as long as standard of care

KEYNOTE-177, a randomized phase III clinical trial evaluated the efficacy and safety of pembrolizumab vs standard of care [chemotherapy ± bevacizumab or cetuximab] as first line therapy for patients with microsatellite instability high/mismatch repair deficient [MSI-H/dMMR] metastatic colorectal cancer [mCRC]. patients with MSI-H represent 5% of patients with mCRC. mismatch repair deficiency and MSI-H status predicted clinical benefit of immune checkpoint blockade with pembro and other PD-1 therapies. in phase II studies pembro demonstrated durable anti tumour activity with an acceptable safety profile in previously treated MSI-H mCRC. the study findings included superior progression free survival [PFS] with pembrolizumab vs chemo - doubling PFS by a median of 16.5 months with pembro vs 8.2 months with standard of care.

a total of 307 patients with MSI-H/dMMR mCRC were randomly assigned 1:1 with 153 patients assigned and treated with pembrolizumab as first line treatment and 154 assigned and 143 receiving chemotherapy with or without targeted therapy, which is best treatment currently known.

the 12 and 24 month PFS rates were 55.3% and 48.3% with pembro vs 37.3% and 18.6%. confirmed overall response rate [ORR] 43.8% vs 33.1% with median duration of response not achieved with pembro vs 10.6 months with chemo.

treatment with pembrolizumab also worked longer - the 24 month response duration with pembro was 83% compared to 35% for chemo, and caused fewer side effects - with 22% of patients having a grade 3 or higher adverse event [AE], compared with 66% in patients who received chemotherapy.

conclusions- pembrolizumab provided a clinically meaningful and statistically significant improvement in PFS vs chemotherapy in patients with MSI-H mCRC. responses were more durable and had an improved safety profile.

what does this mean - pembrolizumab should be the new standard of care as first line therapy in patients with MSI-H mCRC

THIS STUDY DEMONSTRATES A HUGE BENEFIT IN FIRST LINE THERAPY WITH PEMBROLIZUMAB AND TRIAL RESULTS WILL CHANGE CLINICAL PRACTICE CREATING A NEW STANDARD OF CARE FOR MSI-H MCRC

maintenance avelumab + best supportive care [BSC] versus BSC alone after platinum based first line chemotherapy in advanced urothelial carcinoma [UC]. JAVELIN bladder 100 phase III interim analysis. abstract LBA1

adding avelumab after chemotherapy has a very strong overall survival benefit for patients with advanced bladder cancer

urothelial carcinoma [UC] is the 6th most common cancer in the US [200,000 death globally in 2018] and the most common type of bladder cancer. most patients with advanced disease control it with first line platinum based chemotherapy, with short PFS and OS due to chemotherapy resistance. after first line chemotherapy only 25-55% of patients receive second line treatment. *outcomes with second line therapy remain suboptimal because of rapid disease progression.*

PD-L1/PD-1 inhibitors are standard second line treatment for patients with disease progression after platinum based chemotherapy - with only a minority of patients obtaining a durable clinical benefit with second line treatment- with resistance occurring quickly and median overall survival short.

JAVELIN Bladder 100 is a randomized phase III clinical trial - patients have advanced or metastatic urothelial cancer with a response or stable disease with standard first line chemo [gemcitabine and cisplatin or gemcitabine and carboplatin] between four and six cycles of chemo was given - patients were randomized within 10 weeks of completion of chemotherapy and received avelumab or best supportive care.

DISEASE CONTROL ACHIEVED W/CT MAY PROVIDE TIME FOR IO TO HAVE AN ANTI TUMOUR EFFECT

the study included 700 people with locally advanced or metastatic urothelial carcinoma that could not be treated with surgery - 50% of patients had visceral metastasis, approximately 50% being biomarker [PD-L1] positive, approximately 50% having gemcitabine and cisplatin, the majority of patients responding to first line chemotherapy. many similarities existed between the biomarker positive population and the overall population- data showed that the PD-L1 positive population was less likely to have non visceral metastasis.

- initiating IO before disease progression occurs may result in MORE pts receiving tx. —

after 19 months of median follow up, 24% of patients continued on avelumab and 7% on best supportive care- with disease progression the most common cause for discontinuation. overall survival [OS] in the ITT population with avelumab and best supportive care is 21 months vs 14 months for best supportive care. OS in the PD-L1 population also favoured avelumab. median OS not yet reached with avelumab vs 17 months for BSC. OS in the ITT population and PD-L1 positive is statistically significant. landmark survival at 18 months was 70% for avelumab + BSC - key subgroups [different types of chemotherapy, best response to first line chemo and the presence and absence of visceral metastases] also broadly favoured avelumab. at 12 months 30% of patients remained progression free, with 36% remaining progression free at 12 months

CONFIRMED ORRs ARE CHALLENGING TO INTERPRET IN THIS POPULATION B/C OF INITIAL CT TX.

in the PD-L1 positive population. complete response rate [CR] was 6% in the overall population and 10% in the PD-L1 positive population.

61% of patients in the best supportive care arm received subsequent therapy, 43% received immune checkpoint inhibitors [ICI]. and this increased to 75% and 72% respectively in those individuals who progressed.

treatment emergent adverse events were in line with what was expected with ICI- 12% of patients discontinued therapy for treatment related adverse events and two treatment related deaths occurred in the avelumab arm, hypothyroidism was the most commons side effect, and no grade 4 or 5 AEs were observed and only 9% received corticosteroids.

conclusions- the addition of avelumab maintenance to supportive care showed significantly longer overall survival in both the overall population and the PD-L1 positive population. OS was longer with avelumab vs control across all respecified subgroups. the safety profile of avelumab as first line maintenance was manageable and consistent with previous studies.

what does this mean- avelumab first line maintenance in patients whose disease has not progressed with platinum based induction chemotherapy represents a new first line standard of care for advanced UC.

INSTEAD OF WAITING FOR DISEASE TO PROGRESS AFTER CHEMOTHERAPY–WHICH IT DOES IN A LARGE PORTION OF THE POPULATION WITH ADVANCED UROTHELIAL CANCER–ADDING AVELUMAB SIGNIFICANTLY IMPROVES SURVIVAL

the pediatric precision oncology study INFORM. clinical outcome and benefit for molecular subgroups abstract LBA10503

algorithm for targeted precision oncology in refractory or relapsed pediatric cancers in the real world setting are feasible

refractory, relapsed and progressive high risk pediatric oncology patients have a poor prognosis. INFORM is a prospective non interventional, multi centre, multi national feasibility registry with an objective to assess feasibility of pediatric precision oncology in a real world setting.

researchers were able to determine an algorithm to identify molecular targets in certain R/R pediatric cancers

a molecular target priority algorithm was investigated and assessed for clinical benefit. the algorithm consists of seven priority levels from very low to very high based on drug ability, genetic change, expression for the genetic change, the direct drug target, the evidence level of the drug target, and entity specific.

PTS WERE GIVEN TARGETED THERAPIES CREATING ↑ PFS OF 3 MONTHS IN A SMALL GROUP OF CHILDREN W/ RECURRING CANCER

patients from eight countries, with refractory, relapsed progressive malignant disease but, also, exceptional high risk cases at primary diagnosis could participate in this study - with primary diagnosis occurring before the age of 21. fresh, frozen tumour and blood for germline analysis was submitted to KiTZ. identified alterations were discussed on a weekly online interdisciplinary molecular tumour board, which also included the treating physician. all identified alterations were reported in a remote entry database, where, at the same time, clinical follow up was documented, and the treating physician could use the molecular information for clinical decision making. virtual genome sequencing, exome sequencing, RNA sequencing, gene expression, and 850K methylation array were performed.

526 patients with a completed follow up of at least two years are analyzed in this study. of the patients in the study, 8% had a very high priority target [targets included ALK, BRAF, and NRAS mutations, and MET and NTRK gene fusions], 14.8% had a high priority target, 20.3% had a moderate priority target, 23.6% had an intermediate priority target, 14.4% had a borderline priority target, 2.5% had a low priority target, and 1% had a very low priority target. another 15.4% of patients had no actionable target.

USING data collected from tumour samples researchers developed an algorithm that would search for genetic or molecular characteristics in tumours that could potentially be matched to an existing approved or experimental drug

149 patients received a matching targeted therapy and 377 were not matched.

the analysis found that among those with very high priority targets, progression free survival [PFS] was a median of 204.5 days, compared with 114 days. for other priority levels .who received a matching drug median PFS was 118 days vs 116 days. overall survival [OS] in this group was 302 days vs 287 days and in the very high priority group 354 days vs 287 days. improving OS in very high priority children for 67 days.

conclusions- the prioritization algorithm identifies subgroups benefitting from a treatment with matched drugs. researchers were able to identify germline alterations, of importance for patients and families. more diagnostic precision in clinical decision making in collaboration with the treating physician- this will be evaluated further. also, for a large proportion of patients without a very high priority target, further layers of molecular and functional data needs to be incorporated in future programs [functional drug sensitivity profiling, proteomics, liquid biopsies]. there is, however, an urgent need for biomarker driven pediatric interventional clinical trials.

what does this mean - precision medicine is not yet regularly used to treat pediatric cancers- this study shows that there are potential targets in recurrent pediatric cancer that can be used to guide treatment planning. while the study did not significantly improve outcomes for pediatric patients, pediatric precision oncology in a real world setting is feasible, with the prioritization algorithm identifying subgroups that benefited from matched targeted regimen to improve overall survival.

THIS REGISTRY HAS OPENED UP THE GENOMIC LANDSCAPE IN PEDIATRIC ONCOLOGY PROVIDING A UNIQUE SOURCE OF INFORMATION TO HELP MATCH NEW DRUGS OR DRUG IDEAS WITH SUITABLE BIOMARKERS IN CERTAIN PEDIATRIC POPULATIONS

avelumab in patients with gestational trophoblastic tumors resistant to monochemotherapy: final outcomes of TROPHIMMUN phase II trial, cohort A abstract LBA6008

avelumab shows promise in potentially curing gestational trophoblastic tumour after chemotherapy resistance

gestational trophoblastic tumours [GTT] are rare tumours developed in the placenta during pregnancy - low risk GTT is treated with single agent chemotherapy [methotrexate regimen or actinomyocin D] with approximately 70% hCG normalizations and disease cures. in the case of resistance - patients are switched to another single agent chemotherapy or polychemotherapy. polychemotherapy is associated with high cure rate but significant, immediate and long term toxicity. *in the context of current development of neuro targeted agents, there is a need for innovative treatments in GTT patients*.

the primary objective of the TROPHIMMUN trial - an open academic phase II /III trial - was to assess the efficacy and avelumab in GTT patients who have resistance to chemotherapy - in cohort A patients with resistance to mono chemotherapy and cohort B with patients to resistance to polychemotherapy. with a primary endpoint of a rate of successful hCG

normalization, enabling treatment discontinuation. a secondary objective included the safety profile of avelumab as well as resistance free survival and overall survival.

between 2016 and 2017, 17 patients were enrolled, 15 were treated [median age 34 years] with a median follow up of 25 months. 47% of patients at stage III presented with lung metastases.

hCG normalization and avelumab discontinuation occurred in eight patients, including seven patients who had normalized hCG during treatment + one normalization post treatment with avelumab. within 29 months of follow up no patients presented with suspected relapse despite avelumab discontinuation. the seven patients who had resistance to avelumab were successfully treated with subsequent second single agent chemotherapy or polychemotherapy with or without surgery. five patients who presented with resistance to both single agents were successfully treated with avelumab bypassing toxicity related to polychemotherapy.

one year post avelumab discontinuation a patient was able to stop contraception and become pregnant- this is the first report of a health pregnancy in a patient previously treated with immunotherapy.

median resistance free survival was not reached and the four month resistance free survival was 73% with overall survival at 100%. toxicity profile was satisfactory - 93% of patients experienced adverse events - mostly grade 1 - and no dose reduction or treatment delay was needed.

conclusion - this is a first trial of immunotherapy in GTT patients and demonstrates the feasibility of a trial in such a rare tumour. it provides data about the efficacy of avelumab in GTT patients with resistance to single agent chemotherapy - with 50% of patients experiencing successful hCG normalization without relapse despite discontinuation, with a 29 month follow up, meaning these patients are likely cured, with excellent tolerability vs polychemotherapy.

what does this mean- avelumab shows promise as an effective treatment option for GTT that has become resistant to first line chemotherapy. toxic polychemotherapy was avoided for 33% of patients and normal subsequent pregnancy was seen in at least one patient. avelumab is a new therapeutic option for GTT and will be further studied in first line setting.

THIS PROOF OF CONCEPT STUDY SHOWS THAT TREATMENT WITH THE IMMUNOTHERAPY AVELUMAB WORKS AGAINST THESE TUMOURS WHEN RESISTANCE TO SINGLE AGENT CHEMOTHERAPY DEVELOPS

osimertinib as adjuvant therapy in patients with stage IB–IIIA EGFR mutation positive [EGFRm] NSCLC after complete tumour resection. ADAURA. abstract LBA5

osimertinib delays recurrence for non small cell lung cancer [NSCLC] with an EGFR mutation

THE TRIAL WAS UNBLINDED 2YRS EARLY DUE TO THE UNEXPECTED EVIDENCE OF OVERWHELMING EFFICACY

lung cancer is the leading cause of death, accounting for more than 1.7 million deaths annually worldwide. non small cell lung cancer [NSCLC] represents 85% of all lung cancer cases, with an estimated 30% of patients presenting resectable disease at diagnosis. surgery is the primary treatment for patents with early stage NSCLC. adjuvant cisplatin based chemotherapy is recommended for patients with resected stage II/IIA NSCLC and select patients with IB disease.

post operative chemotherapy is associated with only 5% survival benefit and a 6% survival benefit at five years amongst patients with early stage disease. rates of disease recurrence or death following surgery and adjuvant chemotherapy remain high.

osimertinib is now considered the standard of care for first line EGFR mutation positive advanced NSCLC and its demonstrated tolerability suggests that it may be an effective treatment for EGFRm+ early stage NSCLC.

THE PBO ARM IS A REMINDER THAT DESPITE SUCCESSFUL SURGERY + CT AS APPROPRIATE THERE REMAINS A HIGH DEGREE OF DISEASE RECURRENCE IN EARLY STAGE LUNG CANCER

ADAURA is a phase III double blind study assessing the efficacy and safety of osimertinib vs placebo [PBO] in patients with stage IB-IIIA with an epidermal growth factor receptor [EGFR] mutation in NSCLC after complete tumour resection and adjuvant chemotherapy, when indicated. the primary endpoint was disease free survival [DFS] in patients with stage II and IIIA disease with a secondary endpoint of DFS in the overall population with stage IB, II or IIIA. 682 patients were randomized 1:1 with a planned treatment duration of three years. treatment could continue until disease recurrence, treatment completion or discontinuation.

DFS BENEFIT WAS SEEN CONSISTENTLY ACROSS ALL PATIENT SUBGROUPS

the primary endpoint of ADAURA was met with osimertinib demonstrating superior disease free survival versus placebo in patients with stage II to IIIA disease - an 83% reduction in the risk of disease recurrence or death with osimertinib. at one year the DFS was 97% vs 61% in PBO arm. two year disease free survival [DFS] rate was 90% compared to 44% for PBO and three year DFS 80% vs 28% PBO.

the secondary endpoint of DFS in overall stage IB, II and IIIA population was also met - within the lower risk patients at stage IB. a 79% reduction in risk of disease recurrence or death with osimertinib was observed. at two years 89% of patients who received osimertinib were disease free compared to 53% in the placebo arm.

DISEASE RECURRENCE IS REPORTED IN APROX. ½ OF PTS W/ STAGE I DISEASE - 2/3 IN PTS W/ STAGE II AND 3/4 IN PTS W/ STAGE III DISEASE

consistent benefit was also observed regardless of whether patients received prior adjuvant chemotherapy. DFS rates were remarkably high and consistent across stages IB, II and IIIA at 87%, 91% and 88% respectively in contrast to decreasing DFS rates in the placebo arm at two years.

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IT REMAINS CLEAR THAT THERE IS AN UNMET NEED FOR NOVEL AND EFFECTIVE ADJ. THERAPIES TO IMPROVE CLINICAL OUTCOMES IN EARLY STAGE NSCLC

the safety profile observed for osimertinib in this setting was tolerable and consistent with a known profile for osimertinib with no adverse events leading to death.

conclusions- adjuvant osimertinib is the first targeted agent in a global randomized trial to show a statistically significant and clinically meaningful improvement in disease free survival in patients with stage IB, II, or IIIA EGFR mutation positive nonvsmall cell lung cancer. a 79% reduction in the risk of disease recurrence or death with osimertinib was observed and disease free survival rates at two years were 89% vs 5% in the placebo arm. patients had benefit regardless of prior adjuvant chemotherapy.

what does this mean - adjuvant osimertinib provides a highly effective, practice changing treatment for patients with stage IB, II and IIIA EGFRm NSCLC after complete tumour resection. new data will likely change the way physicians treat these early-stage lung cancer patients. these numbers are totally unprecedented and reaffirms approaches to earlier therapy.

RESULTS LIKE THIS ARE SO PROFOUND FOR PATIENTS PROVIDING AN OVERWHELMING BENEFIT FOR PATIENTS WITH EARLY STAGE DISEASE

PROMISING CLINICAL DATA

phase II study of pevonedistat + azacitidine versus azacitidine in patients with higher risk myelodysplastic syndromes [MDS]/chronic myelomonocytic leukemia [CMML], or low blast acute myelogenous leukemia [LB AML] [NCT02610777] abstract 7506

combination of pevonedistat + azacitidine suggests clinically meaningful benefit higher risk myelodysplastic syndromes [HR MDS]

results from the phase II pevonedistat + azacitidine trial - which evaluated pevonedistat plus azacytidine compared to azacytidine alone in rare leukemias, including higher risk myelodysplastic syndromes [HR-MDS] were presented. the data showed the combination suggested benefits in the HR-MDS subgroup across multiple clinically meaningful endpoints, including overall survival [OS], event free survival [EFS] and overall response rates [ORR].
median OS in higher risk MDS 23.9 vs 19.1 months. EFS 21 months vs 16.6 months in the ITT population and in the HR MDS 20.2 months vs 14.8 months was observed with an overall response rate 71% vs 60%

BARCODE 1. a pilot study investigating the use of genetic profiling to identify men in the general population with the highest risk of prostate cancer to invite for targeted screening. abstract 1505

genetic profiling through saliva testing can be adopted as a prostate cancer screening program in general practice

the use of genetic profiles to guide prostate cancer [PrCa] screening is attractive; it requires a one off test utilizing germline DNA which can be assessed for risk loci which are constant, unlike PSA which fluctuates. the results of the BARCODE1 study will be important in defining the role of genetic profiling in targeted PrCa population screening.

association of detectable levels of circulating tumor DNA [ctDNA] with disease burden in prostate cancer [PC]. abstract 5562

ctDNA could be a clinically relevant metric for monitoring response to therapy

a novel computational approach to detect ctDNA leveraging copy number aberrations across the whole genome was tested and sought to confirm its association with disease burden and clinical outcome. significant associations between the level of the measure of tumour burden in the group of patients who are ctDNA positive versus those for ctDNA negative were observed. for clinical outcomes, overall survival was tested and significantly worse outcomes for the ctDNA positive population were seen.

a phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01 abstract 4000

trastuzumab deruxtecan [T-DXd; DS-8201] in patients with HER2 mutated metastatic non small cell lung cancer [NSCLC]. interim results of DESTINY-Lung01 abstract 9504

trastuzumab deruxtecan [T-DXd; DS-8201] in patients with HER2 positive advanced gastric or gastroesophageal junction [GEJ] adenocarcinoma. a randomized, phase II, multicenter, open-label study [DESTINY-Gastric01] abstract 4513

new data points to expand use of the HER2-targeted antibody drug conjugate beyond its approved indication in metastatic breast cancer, including colorectal, lung and gastric cancers

trastuzumab deruxtecan [T-DXd] demonstrated remarkable activity in patients with HER2-expressing mCRC refractory to standard therapies, with a safety profile consistent with previous results. clinical trial information NCT03384940

T-DXd demonstrated promising clinical activity with high ORR and durable responses in patients with HER2-mutated NSCLC. the safety profile was generally consistent with previously reported studies. clinical trial information NCT03505710.

T-DXd demonstrated statistically significant and clinically meaningful improvements in ORR and OS compared with standard chemotherapy [paclitaxel or irinotecan] in patients with HER2+ advanced gastric or GEJ adenocarcinoma. clinical trial information NCT03329690.

T-DXD IS A NOVEL ANTIBODY DRUG CONJUGATE [ADC] ACHIEVING HIGH RESPONSE RATES AND DURABLE RESPONSES FOR HEAVILY PRETREATED PATIENTS

CELL THERAPIES

update of CARTITUDE-1. a phase Ib/II study of JNJ-4528, a B cell maturation antigen [BCMA]-directed CAR T cell therapy, in relapsed/refractory multiple myeloma abstract 8505

early, deep, and durable response at a low dose of CAR T cells observed in heavily pretreated patients

JNJ 4528 is a structurally differentiated chimeric antigen receptor T cell therapy - containing a CD3 zeta signalling domain and a 4-1BB co stimulatory domain. it also contains two BCMA targeting single chain antibodies designed to confirm avidity. CARTITUDE-1 is a phase Ib/II study. the primary objective of the phase I is to characterize the safety and confirm the phase II dose, as informed by the LEGEND-2 study. the phase II primary objective is to evaluate the efficacy of JNJ-4528.

HEAVILY PRE TREATED PTS W/ MEDIAN OF 5 PRIOR THERAPIES

86% of patients had prior autologous transplantation. 100% of patients were triple exposed, and 76% were penta exposed. 86% of patients were triple refractory, and 97% of patients were refractory to the last line of therapy. 93% of patients experienced grade I/II cytokine release syndrome [CRS].

researchers observed an overall response rate of 100% with stringent complete remissions of 86%, and 97% very good partial remissions. overall response rate [ORR] and depth of response were independent of BCMA expression on myeloma cells at baseline. the median time to first response was one month and three months to complete remission. at median follow up of 11.5 months 22 of 29 patients are alive and progression free - three patients died - one from CRS, one from unrelated disease and the third from progression of myeloma. PFS at nine [9] months was 86%.

of note- patients were heavily pretreated with median prior lines of therapy five. 86% of patients had prior autologous transplantation. 100% of patients were triple-exposed, and 76% were penta exposed. 86% of patients were triple refractory, and 97% of patients were refractory to the last line of therapy. clinical trial information NCT03548207.

JNJ 4528 has received breakthrough therapy designation by the FDA

ALL PATIENTS RESPONDED TO TREATMENT

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phase I study of teclistamab, a humanized B cell maturation antigen [BCMA] x CD3 bispecific antibody, in relapsed/refractory multiple myeloma [R/R MM] abstract 100

early data shows durable response for heavily pretreated patients

despite recent advances and new therapies, patients outcomes are poor once available classes of therapies are exhausted- this is especially true as patients progress through proteasome inhibition [PI] immunomodulatory drug therapies. in patients refractory to these existing therapies, the median overall survival [OS] can be between 6 to 11 months.

teclistamab is a bispecific BCMA x CD3 antibody that induces T cell mediated cytotoxicity against BCMA expressing myeloma cells. patients had received a median six lines of prior therapy. 97% of patients were triple class exposed, 83% triple class refractory and 38% penta drug refractory.

an overall response rate of 67% was observed in patients with advanced RRMM with 16/21 patients having ongoing response with a safety profile that was manageable across all doses.
this data supports further evaluation of teclistamab in expansion cohorts. clinical trial information NCT03145181

BCMA AND CD3 BISPECIFIC ANTIBODY APPROACHES OFFER AN OFF THE SHELF, IMMUNE MEDIATED THERAPY FOR PATIENTS

first in human data of ALLO-501 and ALLO-647 in relapsed/refractory large B cell or follicular lymphoma [R/R LBCL/FL]. ALPHA study abstract 8002

encouraging results, showing the feasibility of a widely available, on demand CAR T treatment for patients with advanced blood cancer.

allogenic- or off the shelf, chimeric antigen receptor therapy [CAR T] addresses the logistical challenges and variable product quality of autologous CAR T therapy. ALLO 501 is a genetically modified anti CD19 CAR T cell product in which the TCR alpha constant gene is disrupted to reduce the risk of graft versus host disease [GvHD] and the CD52 gene is disrupted to permit the use of ALLO 647, an anti CD52 mAB. this is an open label, phase I trial in adults with R/R LBCL/FL who have received at least two prior lines of therapy, including prior anti CD19 cell therapy [four patients].

among 19 patients treated, 12 responded - 63% ORR including seven patients in whom tumour cells were no longer detectable [37% CR}. one patient who progressed after PR and was re-dosed with ALLO 501.

ALLO CAR T cell expansion was associated with responses observed across all cell dose levels. a best overall response rate of 63%, and best complete response rate of 37% was observed. nine of the 12 responses are currently ongoing with one patient achieving CR after the second infusion of ALLO 501. higher dose ALLO 647 appears to associated with deeper responses [50%. CR]. further follow up is necessary to determine the durability of those responses. clinical trial information NCT03939026

THESE RESULTS SUGGEST THAT THE SAFETY AND THE SHORT TERM EFFICACY IS COMPARABLE TO AUTOLOGOUS CAR T PRODUCTS THAT ARE CURRENTLY IN CLINIC

phase I dose escalation and expansion trial to assess the safety and efficacy of ADP-A2M4 SPEAR T cells in advanced solid tumors abstract 102

anti tumour activity observed across multiple cancers

this study evaluated safety and efficacy of SPEAR T cells directed against the MAGE-A4 peptide expressed in nine tumour types. MAGE A4 is a cancer/testis antigen with expression in many solid tumours promoting cell growth by preventing cell cycle arrest and apoptosis. this phase I dose escalation expansion trial evaluated patients who were HLA*02 [human leukocyte antigen serotype] positive with advanced cancers that expressed the MAGE A4 protein.

analysis included 38 patients with a broad range of tumour types with the most common tumour type being synovial sarcoma. durable responses in synovial sarcoma was observed, with a confirmed response in 50% of patients with a disease control rate of 90%. confirmed responses were also observed in lung and head & neck cancers and tumour reductions in ovarian, bladder and melanoma. based on this synovial sarcoma data, a registrational trial, SPEARHEAD-1, has begun enrolling synovial sarcoma and MRCLS patients at different sites in north america and europe. additional trials of SPEAR T cells targeting MAGE-A4 have been initiated as well. clinical trial information NCT03132922

IMMUNOTHERAPIES

long term follow up of lifileucel [LN-144] cryopreserved autologous tumor infiltrating lymphocyte [TILs] therapy in patients with advanced melanoma progressed on multiple prior therapies abstract 10006

these data demonstrate potential efficacy and durability of response in a patient population with severely limited treatment options

TREATMENT OPTIONS REMAIN LIMITED FOR PTS W/ ADVANCED MELANOMA WHO HAVE PROGRESSED ON ICI OR TARGETED THERAPIES

C-144-01 is a global phase II open label, multicentre study of efficacy and safety of lifileucel in patients with unresectable metastatic melanoma who have progressed on checkpoint inhibitors and BRAF/MEK inhibitors, if *BRAFv600* mutant. tumours were resected at local institutions, processed in central GMP facilities for TIL production, manufactured, cryopreserved and shipped back to sites in a 22-day process. therapy consisted of one week of lymphodepletion, a single lifileucel infusion, and up to 6 IL-2 doses.

mean time to response was 1.9 months - of the 66 evaluable subjects, 24 had an objective response, resulting in an objective response rate of 36.4%. including 3% [2] complete response and 33.3% [22] partial response. an additional 43.9% had stable disease. there was no difference in objective response with regards to age, prior anti CTLA-4 treatment, BRAF mutational status, PD-L1 status of the tumour, or baseline performance status. no discernible association with regards to responsive subjects with the presence of brain and/or liver lesions. nor was there an association of response with time from last infusion of PD-1 antibody therapy. overall, these data indicate that responses from lifileucel therapy are achievable for subjects across a relatively broad range of clinical and pathologic features.

LIFILEUCEL HAS DEMONSTRATED POTENTIAL EFFICACY AND DURABILITY OF RESPONSE FOR PATIENTS WITH METASTATIC MELANOMA AND REPRESENTS A VIABLE THERAPEUTIC OPTION FOR PATIENTS WHO HAVE PROGRESSED ON ALL OTHER AVAILABLE TREATMENT OPTIONS

primary analysis of a randomized, double blind, phase II study of the anti TIGIT antibody tiragolumab plus atezolizumab versus placebo plus atezo as first line treatment in patients with PD-L1-selected NSCLC [CITYSCAPE] abstract 9503

novel inhibitory immune checkpoint TIGIT in combination with PD-L1/PD-1 provide potential for new treatment option

the immunomodulatory receptor TIGIT is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers. anti TIGIT antibodies which prevent TIGIT from binding to its ligand could restore the anti tumour response and could complement the activity of anti PD-L1/PD-1 antibodies.

tiragolumab + atezolizumab showed clinically meaningful improvement in ORR and PFS in the ITT population compared to placebo + atezolizumab. an objective response of 31% for patients treated with tiragolumab + atezolizumab vs 16% for patients treated with placebo + atezolizumab. with median PFS of 5.42 months vs 3.58 respectively. confirmed objective response rates in the ITT patient population showed improved ORR with tira + atezo of 37% vs. 21% with placebo + atezo. likewise, patients whose tumours expressed high levels of PD-L1 had an objective response rate of 66% when treated with tira + atezo versus 24% with placebo + atezo. treatment with tira plus atezo resulted in higher frequencies of adverse events - largely grade I/II in severity.

BRAIN METS

tucatinib versus placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ metastatic breast cancer with brain metastases [HER2CLIMB] abstract 1005

tucatinib shows promise for brain mets

results from an exploratory efficacy analysis of the phase II HER2CLIMB trial showed that tucatinib in combination with trastuzumab and capecitabine extended overall survival [OS] and delayed disease progression in the central nervous system [CNS] for patients with HER2 positive metastatic breast cancer and brain metastases.

patients with brain metastases in the tucatinib arm had a 68% reduced risk of disease progression in the CNS compared with the placebo arm and a nearly 6 month gain in median CNS PFS [9.9 vs 4.2 months]. patients in the tucatinib arm also had a 42% reduced risk of death compared with the placebo arm and an approximately six month gain in overall survival [OS; 18.1 vs 12.0 months]. the intracranial response rate more than doubled with tucatinib compared with placebo.

HER2CLIMB SERVES AS AN EXCELLENT EXAMPLE OF CLINICAL TRIAL ENTRY CRITERIA AND INCLUSION FOR PATIENTS WITH BRAIN METASTASES THAT NEED CLINICAL TRIALS AND WHO NEED NOVEL THERAPEUTICS

BREAST CANCER

chemotherapy de-escalation using an FDG-PET/CT [F-PET] and pathological response adapted strategy in HER2[+] early breast cancer [EBC]. PHERGain trial abstract 503

select HER2-positive early breast cancer patients would not need chemotherapy - favourably improving toxicity profile

in patients with HER2+ early breast cancer, the combination of trastuzumab [herceptin] and pertuzumab [perjeta] has shown promising pathologic complete response [pCR] rates, but is said to still be low compared with the addition of chemotherapy. in PHERGain, researchers sought to identify sensitivity markers to trastuzumab+pertuzumab through early metabolic response, by F-PET, in an effort to de-escalate chemotherapy. results of the study showed that F-PET can identify patients who will likely benefit from a chemotherapy free approach and receive neoadjuvant treatment with trastuzumab and pertuzumab alone.

Nearly 40% of patients who started dual HER2 blockade with trastuzumab + pertuzumab and were PET responders, acheived a total pCR. PET identifies patients with HER2+ EBC who are more likely to achieve a pCR and with trastuzumab based therapy. this chemotherapy [CT] free strategy does not jeopardize breast conserving surgery in HER2+ EBC patients and the omission of CT is associated with a more favourable toxicity profile.

PET IS WIDELY AVAILABLE TOOL THAT CAN BE UTILIZED TO DE-ESCALATE THE NEED FOR CHEMOTHERAPY IN SOME PERSONS WITH EARLY STAGE BREAST CANCER - THIS IS AN IMPORTANT PATIENT CENTERED APPROACH THAT MINIMIZES SIDE EFFECTS.

validation of MAF biomarker for response prediction to adjuvant bisphosphonates in two clinical trials: AZURE and NSABP-B34 abstract 513

these results are evidence towards introducing MAF testing into clinical practice

in this analysis of two pivotal trials of patients with breast cancer, AZURE and NSAPB-B34, researchers evaluated the levels of MAF [a transcription factor of the AP-1 family] amplification status in an effort to determine whether this can serve as a predictive biomarker of response to adjuvant bisphosphonates.

the exploration of samples in both studies showed that MAF amplification *does* predict response to adjuvant bisphosphonates, findings of which can be used as evidence toward introducing MAF testing into breast cancer practice.

BISPHOSPHONATES HAVE A SMALL BUT SIGNIFICANT IMPACT ON BREAST CANCER OUTCOMES- THEY ALSO COME WITH SIDE EFFECTS. BEING ABLE TO IDENTIFY THE POPULATION THAT GETS THE BIGGEST BENEFIT WOULD HELP PERSONALIZE CARE

towards data driven decision making for breast cancer patients undergoing mastectomy and reconstruction. prediction of individual patient reported outcomes at two year follow up using machine learning abstract 520

patient reported outcomes [PRO] plays a crucial role in determining post operative outcomes

post surgical satisfaction with breasts is a key outcome for women undergoing cancer related mastectomy and reconstruction. current decision making relies on group level evidence, which may not offer optimal choice of treatment for individuals.

a validated machine learning algorithm was designed to predict individual post operative breast satisfaction from mastectomy and breast reconstruction - machine learning algorithms were able to accurately predict changes in women's satisfaction with breasts. Baseline satisfaction with breasts was the most informative predictor of outcome, followed by radiation during or after reconstruction, nipple sparing and mixed mastectomy, implant based reconstruction, chemotherapy, unilateral mastectomy, lower psychological well being and obesity.

results showed that such algorithms could be appropriate in identifying those who might benefit from alternative treatment decisions than suggested by group level evidence.

ANOTHER PATIENT CENTERED TRIAL THAT USES PERSONALIZED PREDICTION AROUND BREAST RECONSTRUCTION TO AID IN CLINICAL DECISION MAKING

comprehensive profiling of androgen receptor positive [AR+] triple negative breast cancer [TNBC] patients treated with standard neoadjuvant therapy [NAT] +/- enzalutamide abstract 517

use of treatment approaches based upon molecular profiling of pre treatment biopsies

patients with luminal androgen receptor [AR]+ triple-negative breast cancer [TNBC] are known to have lower pathological complete response [pCR] rates following neoadjuvant chemotherapy. in the nonrandomized ARTEMIS trial, patients who had chemotherapy insensitive TNBC were treated with a regimen of enzalutamide + paclitaxel- this approach led to a 33.3% pCR rate, suggesting that this type of combination may be one to explore in this patient subtype.

A MOVE TOWARDS TARGETING OR TAILORING TREATMENT IN TRIPLE NEGATIVE BREAST CANCER

a randomized phase III trial of systemic therapy plus early local therapy versus systemic therapy alone in women with de novo stage IV breast cancer. a trial of the ECOG-ACRIN research group [E2108] abstract LBA2

early local therapy offers no survival benefit in patients with de novo metastatic breast cancer and an intact primary tumour

the trial included 256 patients who received optimal systemic therapy before being randomly assigned to either continue optimal systemic therapy or receive optimal systemic therapy with loco regional therapy. the results show that there was no significant difference in overall or progression-free survival between the two groups (3-year overall survival rate = 68.4% in the optimal systematic therapy plus loco regional treatment arm vs 67.9% in the optimal systemic therapy alone arm).

although the loco regional therapy arm had a reduced risk of loco regional recurrences/ progression compared with the optimal systemic therapy alone arm, no improvements were seen for health related quality of life [HRQOL]. at 18 months, HRQOL was significantly worse for the loco regional therapy arm. there was no quality-of-life advantage in the group of women who received local therapy to the breast tumour.

one of the reasons for considering surgery and radiation is the idea that growth of the tumour will impair quality of life. instead, the adverse effects of surgery and radiation appear to balance out the gains in quality of life that were achieved with better control of the primary tumour.

WOMEN WHO PRESENT WITH A NEW DIAGNOSIS OF BREAST CANCER ALREADY IN STAGE IV SHOULD NOT BE OFFERED SURGERY AND RADIATION FOR THE PRIMARY BREAST TUMOUR WITH THE EXPECTATION OF A SURVIVAL BENEFIT

MINDACT: Long-term results of the large prospective trial testing the 70-gene signature MammaPrint as guidance for adjuvant chemotherapy in breast cancer patients abstract 506

a long term analysis confirms the clinical utility of MammaPrint - a 70-gene signature assay that can identify which breast cancer patients with a high clinical pathological risk can safely omit adjuvant chemotherapy

among the intent to treat [ITT] population with a median follow up of 8.7 years, patients with high clinical risk but low genomic risk who received adjuvant chemotherapy had a small gain in distant metastasis free survival [DMFS] compared with patients who did not receive chemotherapy [92.0%; vs 89.4%].

a subgroup analysis among hormone receptor positive and HER2 negative patients revealed no difference in DMFS between treatment groups for patients over the age of 50, yet a 5% difference for patients 50 years or younger, favouring treatment with chemotherapy [93.6% vs 88.6%]. DMFS gains seen with chemotherapy for premenopausal patients may be due to a lack of ovarian function suppressant in the non chemotherapy arm.

EVIDENCE FOR THE CLINICAL UTILITY OF THE 70-GENE SIGNATURE FOR ADJUVANT CHEMOTHERAPY DECISION MAKING IS MAINTAINED

GENITOURINARY CANCERS

IMvigor010: primary analysis from a phase III randomized study of adjuvant atezolizumab versus observation in high risk muscle invasive urothelial carcinoma [MIUC] abstract 5000

adjuvant treatment with the PD-L1 inhibitor did not significantly improve disease-free survival [DFS] versus observation in patients with muscle-invasive bladder cancer

IMvigor010 is an international, open label, controlled, phase III trial investigating the efficacy and safety of adjuvant atezolizumab compared with observation in 809 people with muscle invasive bladder cancer [MIUC] who are at high risk for recurrence following surgical resection. IMvigor010, the first phase 3 adjuvant study of a checkpoint inhibitor in MIUC, did not meet its primary end point of DFS. and more treatment discontinuation due to AEs was seen vs mUC studies. no pre specified subgroups, including higher PD-L1 status showed treatment benefit with atezolizumab. OS follow up is ongoing and additional exploratory biomarker and subgroup analyses may warrant further study.

MIUC continues to be a deadly disease despite curative intent treatment.

IT REMAINS DIFFICULT TO REDUCE THE RISK OF MUSCLE INVASIVE UROTHELIAL CANCER AFTER SURGERY. RANDOMIZED CLINICAL TRIALS ARE NEEDED TO ANSWER IMPORTANT QUESTIONS LIKE THIS.

pembrolizumab plus axitinib versus sunitinib as first line therapy for advanced renal cell carcinoma [RCC]. updated analysis of KEYNOTE-426 abstract 5001

follow up pembrolizumab + axitinib continue to provide an OS benefit with an increased rate of complete responses [CR]

earlier data from the KEYNOTE-426 trial demonstrated significantly improved OS, PFS and ORR for the first line treatment of patients with advanced renal cell carcinoma [RCC] [vs sunitinib]. findings with longer follow up, at a median of 27 months continued to demonstrate clinically significant improved efficacy for previously untreated advanced RCC. exploratory landmark analysis demonstrated that greater depth of tumour shrinkage was associated with increased OS.

phase II study of nivolumab and salvage nivolumab + ipilimumab in treatment naïve patients with advanced renal cell carcinoma [RCC] HCRN GU16-260 abstract 5006

optimized management of nivolumab and ipilimumab in advanced renal cell carcinoma [RCC]. a response-based phase II study OMNIVORE abstract 5005

sequencing based studies evaluate strategies with the PD-1 and CTLA-4 inhibitors nivolumab and ipilimumab, respectively in RCC

in the phase II, response adaptive OMNIVORE trial, investigators evaluated the sequential addition of two doses of ipilimumab to induce response in non responders to nivolumab, as well as the duration of nivolumab in responding patients with advanced RCC.

in HCRN GU16-260, the efficacy and toxicity of single agent nivolumab was evaluated in patients with advanced RCC, and then also salvage therapy with nivolumab/ipilimumab in patients whose tumours are resistant to initial nivolumab monotherapy. this study answers an important question of sequencing nivolumab with ipilimumab.

in both studies, little CR were achieved and begs the question of whether using these therapies in combination may be a better approach.

phase II study of the oral HIF-2α inhibitor MK-6482 for von hippel lindau disease associated renal cell carcinoma abstract 5003

initial results of the open label, phase II study of the HIF-2α inhibitor showed promising efficacy and tolerability in patients with VHL associated clear cell RCC and responses in other VHL related lesions, suggesting that the agent can be further explored in VHL disease. these data support further investigation of MK-6482 in VHL disease. clinical trial information: NCT03401788.

VHL DISEASE ASSOCIATED RCC REPRESENTS A VERY SMALL SUBSET OF PATIENTS - WHERE THERE IS AN UNMET NEED FOR PATIENTS

LUNG CANCER

KEYNOTE-604. pembrolizumab or placebo plus etoposide and platinum [EP] as first line therapy for extensive stage [ES] small cell lung cancer [SCLC] abstract 9001

significant improvement of PFS without OS benefit with IO + chemo combo for extensive stage SCLC patients

in the double blind, phase III study, the PD-1 inhibitor pembrolizumab was explored in combination with etoposide and platinum based therapy for treatment naïve patients with extensive stage small cell lung cancer [SCLC].

findings showed that the immunotherapy + chemotherapy combination showed a significant improvement in progression free survival [PFS], but the OS benefit was not found to be significant when compared with placebo and chemotherapy. no unexpected toxicities were observed with the addition of pembrolizumab.

IN OTHER TRIALS THE ADDITION OF THE ANTI PD-L1 ANTIBODY HAVE DEMONSTRATED SIGNIFICANT SURVIVAL ADVANTAGE FOR THE ADDITION OF ANTI PD-L1 BLOCKADE FOR THIS DIFFICULT TO TREAT PATIENT POPULATION

first line tyrosine kinase inhibitor [TKI] with or without aggressive upfront local radiation therapy in patients with EGFRm oligometastatic non small cell lung cancer. interim results of a randomized phase III, open label clinical trial [SINDAS] abstract 9508

findings suggest aggressive local therapy to sites at diagnosis should be explored further in large cohort phase III trials as a standard treatment option in this clinical scenario

researchers explored the activity of upfront stereotactic radiation plus a frontline EGFR TKI in patients with oligometastatic NSCLC in a multi centre, chinese SINDAS trial. the use of this type of regimen demonstrated improved PFS and OS versus a TKI alone, and the data suggest that aggressive local therapy to sites at diagnosis is an approach that should continue to be explored.

the addition of stereotactic radiotherapy to initial TKI significantly improved both PFS and OS. critical review of the presented data will be necessary to see if this should impact current practice but the implications could be significant. clinical trail information NCT03066778

nivolumab + ipilimumab + 2 cycles of platinum doublet chemotherapy vs 4 cycles chemo as first line treatment for stage IV/recurrent non small cell lung cancer [NSCLC]. checkMate 9LA abstract 9501

the combination of nivolumab and ipilimumab, together with a limited course of chemotherapy, should be considered as a new first line treatment opportunity for patients with advanced non-small cell lung cancer

checkmate 9LA is a phase III, randomized study evaluating nivolumab + ipilimumab + 2 cycles of chemotherapy in first line stage IV | recurrent NSCLC. nivolumab + ipilimumab was shown to improve OS and duration of response [DOR] vs chemo in first line in NSCLC regardless of PD-L1 expression [checkmate 227]. researchers hypothesized that a limited course of chemo combined with nivo + ipi could provide rapid disease control while building on the durable OS benefit seen with dual PD-1 and CTLA-4 inhibition.

a clinically meaningful improvement of all efficacy endpoints [primary endpoint OS, secondary endpoints PFS at efficacy related to PDL1 expression stages] was observed and increased with longer follow up - at 12 months follow OS was further improved [63% vs 47%]. 34% of patients in the chemotherapy arm received a subsequent treatment with an immunotherapy following progression of the disease and an interesting survival benefit was seen in the group of patients with brain metastases

based on these data, the FDA granted a priority review designation to the regimen in this setting for patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumour aberrations, with an expected action date of august 6, 2020.

THE COMBINATION OF NIVOLUMAB AND IPILIMUMAB, TOGETHER WITH A LIMITED COURSE OF CHEMOTHERAPY, SHOULD BE CONSIDERED AS A NEW FIRST LINE TREATMENT OPPORTUNITY FOR PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

HEMATOLOGIC CANCERS

carfilzomib, lenalidomide, and dexamethasone [KRd] versus bortezomib, lenalidomide, and dexamethasone [VRd] for initial therapy of newly diagnosed multiple myeloma [NDMM]. results of ENDURANCE [E1A11] phase III trial abstract LBA3

the combination of carfilzomib, lenalidomide, and dexamethasone [KRd] did not show superior efficacy in patients with newly diagnosed myeloma absent a high-risk disease prognosis, compared with the standard of care–bortezomib, lenalidomide, and dexamethasone [VRd]

there was no improvement in progression free survival by replacing bortezomib with carfilzomib in the current standard initial treatment of patients with newly diagnosed standard - or intermediate risk myeloma, even though a higher partial response rate with the carfilzomib combination was observed. more severe cardiac, pulmonary, and renal toxicities with carfilzomib were also observed.

although phase II trial data suggested a better outcome with KRd, compared to historical data with VRd, this has not borne out in the phase III ENDURANCE trial. it also raises concern for toxicities, which need to be carefully monitored for.

THE ENDURANCE STUDY HIGHLIGHTS THE IMPORTANCE OF USING DATA FROM PHASE III TRIALS TO DRIVE CLINICAL PRACTICE

multiple myeloma [MM] vaccination [influenza, FV and pneumococcal, PV] rates worldwide and impact on infection, hospitalization, and death abstract 8528

as MM patients are living longer, with prolonged exposure to systemic therapy, there is a need to vaccinate and to determine the effectiveness of these vaccines - especially in the current global context

the INSIGHT MM study was designed to better understand patient and disease characteristics in multiple myeloma both at diagnosis and at relapse, as well as treatment patterns, clinical outcomes, and treatment-associated tolerability, effectiveness, quality of life, and healthcare resource utilization. MM is a cancer of the immune system and infections are common reasons for hospitalization and death in MM. the study enrolled 4318 patients from 15 countries, who are being followed up prospectively for at least five years.

researchers analyzed influenza [FV] and pneumococcal [PV] patterns and associated clinical outcomes in INSIGHT MM, the largest global, prospective, observational study in myeloma to date. and assessed the association between vaccination status and healthcare resource utilization [HRU] and deaths due to infections and OS.

findings showed that global vaccination rates for MM patients were low and varied by region. the US reported the highest vaccination rates and the lowest rate of deaths due to infections.

conversely, asia had the lowest FV and PV rates and the highest incidence of deaths due to infections. lack of FV was associated with with higher rated of hospitalization and hospital admissions due to infections. rate of death due to infections was lower among vaccinated vs non vaccinated patients. univariate analysis showed that patients had poorer OS if they did not receive FV or PV. racial and other disparities should be investigated in relation to vaccination access.

vaccination is important in MM and should be encouraged

IN A POST-COVID-19 WORLD, THE ROLE OF INFECTIONS IN CANCER WILL BECOME INCREASINGLY IMPORTANT

HealthTree patient portal mediated myeloma patient reported vaccination and antibiotic use abstract e20567

anti microbial prophylaxis may improve patient outcomes, but real world use has not been well characterized. HealthTree [healthtree.org] was created by myeloma patient jenny ahlstrom

multiple myeloma [MM] is a cancer of the immune system with infection a major cause of morbidity and mortality. vaccines are the first line of prevention for infectious diseases. an investigator submitted online survey asking about infection prophylaxis and vaccinations was fielded to 4,944 patients. 458 patients participated in the surveys.

both FV and PV were fairly high in the self selected cohort vs global registries. patient reported interventions via an online portal can help investigators survey the patient community and result in hypothesis generating research questions including investigating vaccine: types, dosing, sequencing, and use of anti infective interventions.

HealthTree patient portal mediated myeloma patient reported diagnostic imaging and pathology testing abstract e20565

HealthTree is an online portal for patients with multiple myeloma to find optimal treatment options and help identify a cure; the platform also serves as a database for the research community. it is the largest single database of patients with myeloma.

MM prognostic risk factors include cancer genetics as well as imaging characteristics- in order to engage the patient community regarding genetic testing and diagnostic imaging a patient centered platform, HealthTree was utilized to evaluate the patient understanding of cancer genetic characteristics as well as evaluation of radiology methods used to evaluate their disease.. 558 patients participated. real or perceived gaps in optimized genetic and imaging testing exist, which may reflect a communication or education gap. patient reported interventions via an

online portal can help investigators survey the patient community and result in hypothesis generating research questions including the actual use of testing, communication and education about testing and testing options, and MD trends in testing.

USING AN ONLINE PORTAL LIKE HEALTHTREE CAN HELP INVESTIGATORS LEARN FROM REAL-WORLD DATA IN THE PATIENT COMMUNITY AND RESULT IN THE DEVELOPMENT OF NEW HYPOTHESES AND RESEARCH QUESTIONS

DREAMM-6. safety and tolerability of belantamab mafodotin in combination with bortezomib/dexamethasone in relapsed/refractory multiple myeloma [RRMM] abstract 8502

the DREAMM-6 trial was designed to explore the benefit of antibody drug conjugate [ADC] belantamab mafodotin in combination with standard of care therapies, lenalidomide and dexamethasone, bortezomib and dexamethasone. the ongoing, two part, two arm trial is investigating the safety, tolerability, and clinical activity in patients with relapsed/refractory myeloma [RRMM] previously treated with at least one prior line of therapy. early data from part 1 of the trial looking at the ADC added to bortezomib/dexamethasone showed a tolerable safety profile.

50% of the patients achieved a deep response with a clinical benefit rate of 83%. as these data mature, researchers will learn whether these responses deepen further over time, and how durable treatment responses are, but this early snapshot of these responses is extremely encouraging.

to note. there were four abstracts on the anti BCMA antibody drug conjugate [ADC] belantamab mafodotin [GSK2857916] and two trials in progress abstracts, DREAMM-5 abstract TPS8552 and DREAMM-9 abstract TPS8556 in the DREAMM series of clinical trials. clinical trial information: NCT03544281.

THESE DATA PROVIDE INFORMATION ABOUT A NOVEL DRUG THAT WILL LIKELY BE AVAILABLE IN THE CLINICAL SETTING- SOON

GASTROINTESTINAL CANCERS

SWOG S1505. results of perioperative chemotherapy with mFOLFIRINOX versus gemcitabine/nab-paclitaxel [Gem/nabP] for resectable pancreatic ductal adenocarcinoma [PDA] abstract 4504

data showed that neither regimen particularly improved OS over the other

the prospective, phase II SWOG S1505 trial evaluated perioperative mFOLFIRINOX versus gemcitabine/nab-paclitaxel in patients with resectable pancreatic ductal adenocarcinoma [PDAC], a patient population that typically has suboptimal outcomes after curative treatment. patients with clearly resectable PDAC were randomized to receive perioperative mFOLFIRINOX or gemcitabine/nab-paclitaxel with a primary outcome of two year OS. this study confirmed no difference in outcome between the two arms.

this study also exemplified the many challenges patients with PDAC encounter with toxicities and with less than half of patients enrolled able to complete all planned therapy. the median OS in both arms underperformed historical controls, including single agent gemcitabine control arms [~30 months].

trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 over expression: NRG Oncology/RTOG 1010 abstract 4500

the addition of trastuzumab to trimodality treatment did not improve DFS for patients with HER2 over expressing esophageal adenocarcinoma

investigators sought to determine whether trastuzumab increases DFS when combined with trimodality treatment [CRT] for patients with HER2 over expressing esophageal adenocarcinoma.

the addition of this approach did not improve DFS in this patient population. the primary end point of this study was median DFS, and the study failed to show an improvement. clinical trial information NCT01196390.

overall survival [OS] and long term disease free survival [DFS] of three versus six months of adjuvant oxaliplatin and fluoropyrimidine based therapy for patients with stage III colon cancer [CC]. final results from the IDEA [international duration evaluation of adj chemotherapy] collaboration abstract 4004

clinical meaningfulness of findings should be widely and consistently adopted worldwide

the objective of the study is to evaluate the non inferiority of 3 month vs 6 month treatment with adjuvant FOLFOX/CAPOX for patients with stage III colon cancer- the results presented on the primary endpoint of disease free survival [DFS] with mature data - median six years. three year DFS and two secondary endpoints [5yr OS and DFS] show minimal, clinically irrelevant differences for most patients with stage III colon cancer using 3 months of adjuvant therapy.

the IDEA collaboration study showed in the first pooled analysis of its primary end point for DFS, that CAPOX for 3 months was as effective as 6 months in the adjuvant treatment of patients with stage III colon cancer. importantly, there were less toxicities, and more specifically significantly less lifelong debilitating neuropathy in the 3 month treated arm. minimal loss of efficacy with 3 months CAPOX in high risk and 3 months FOLFOX in low risk cancers was observed as well as relevant loss with 3 months FOLFOX in high risk cancers.

the study data concludes that there was a strong correlation between three year DFS and five year OS data. clinical conclusions primarily that the difference in five year overall survival between three and six months is minimal, however the difference in toxicity is very large, and the overall survival of stage III colon cancer is very high, 83% at five year, which is much higher than historically.

implications for clinical practice are that 60% of patients with stage III colon cancer are low risk and should receive 3 months of CAPOX. the other 40% of patients are high risk. for the majority of these, the risk benefit assessment suggests 3 months of CAPOX as well. for those unwilling to lose even 1% to 2% of efficacy, 6 months of therapy is recommended.

THE FINDINGS UNMITIGATEDLY SUPPORT THE USE OF THREE [3] MONTHS OF ADJUVANT CAPOX AS THE STANDARD FOR THE VAST MAJORITY OF STAGE III COLON CANCER.

a randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study abstract 4005

the role of perioperative therapy for clearly resectable liver-only metastases [LM] from colorectal cancer [CRC] remains a subject of debate

patients with liver only metastases [LM} from colorectal cancer have an unclear outcome from adjuvant chemotherapy following hepatectomy. in this phase II/III trial, researchers compared the use of adjuvant mFOLFOX6 versus hepatectomy alone. results showed that the addition of mFOLFOX6 improved DFS, but this did not correlate with OS, suggesting the added treatment is not beneficial. the study suggested a trend for DFS benefit, but a detriment for OS - therefore the authors concluded that postoperative FOLFOX should not be administered in patients who undergo resection for LM in CRC.

results from EORTC 40983 [EPOC] suggested a modest DFS benefit from administration of perioperative FOLFOX versus no therapy, with no meaningful change in five year rate of OS.

the new EPOC study assessed the role of cetuximab plus FOLFOX versus FOLFOX in the perioperative setting, and found a concerning detrimental effect from the addition of cetuximab to FOLFOX.

data from three different randomized trials over the last 10 years suggest that it is reasonable to recommend that the best standard for patients with clearly resectable LM in CRC is surgery only. the role of perioperative or postoperative treatment with FOLFOX at best may improve DFS but not OS, with a potential detriment to OS –especially with the addition of cetuximab

MELANOMA

a phase II study to evaluate the need for > two doses of nivolumab + ipilimumab combination [combo] immunotherapy abstract 10003

preliminary data suggest immunologic effects occur after dose one and do not further increase after dose two

standard of care nivolumab + ipilimumab is given in four doses in patients with unresectable stage III/IV melanoma, whether four doses are needed is questionable given that retrospective data suggests patients receiving less than four doses can have durable benefit with decreased toxicity.

at week six - 68% [41] of patients had favourable anti tumour effect [FATE] with best overall response rates at week 12 or any time afterwards were 48% and 53% respectively. if patients achieved no tumour burden growth or tumour shrinkage they continued with maintenance nivolumab alone. if patients did not meet this pre specified six week protocol criteria or had tumour growth [over 4%] or any new lesions they continued to receive standard of care dosing nivolumab in combination with ipilimumab with two additional doses.

18%, 58%,12% and 10% had one, two, three, four doses of the combo respectively. at median follow up of 11 months - any grade treatment related toxicity occurred in 100% of patients. 32% [19] of the patients who did not achieve FATE at six weeks had no response with ongoing combo dosing.

the first two doses of nivo + ipi appear to drive the combo's response efficacy and toxicity -. further research is needed to understand which patients are most likely to benefit from fewer doses as well as the safety and efficacy of one dose of nivolumab + ipilimumab

autoantibodies as predictors for survival and immune related adverse events in checkpoint inhibition therapy of metastasized melanoma abstract 10011

this study yielded novel and interesting autoantibody targets in melanoma patients - with some autoantibodies linked to clinical outcome and/or irAEs

increasing evidence suggests that the B cell response in cancer patients is an important component of anti tumour immunity. autoantibodies targeting tumour and self antigens may serve as biomarkers of anti tumour and auto immunity. as they can be measured in patient' sera, they have great potential as clinical routine biomarkers. the objective of this study was to explore if autoantibodies are associated with survival and immune related adverse events [irAE] in patients with metastatic melanoma under checkpoint inhibitor [ICI] therapy.

in this study tumour samples were assessed from advanced melanoma patients who had received ICI treatment. from a wide range of autoantibodies, the study achieved identifying

those that were most frequently correlated with the risk of immune related adverse events as well as the probability of treatment response. further validation studies are needed.

THE KNOWLEDGE OF HOW TO OPTIMALLY BENEFIT FROM ICI BASED THERAPIES IS STILL GROWING, AND WITH THE SUPPORT OF NEW BIOMARKERS SUCH AS AUTOANTIBODIES, PHYSICIANS, REGULATORS AND REIMBURSERS COULD PROVIDE SAFER GUIDANCE TO USING ICIS WITHOUT COMPROMISING EFFICACY IN MELANOMA

significant antitumour activity for low dose ipilimumab with pembrolizumab immediately following progression on PD1 Ab in melanoma in a phase II trial abstract 10004

this study of pembrolizumab + ipilimumab demonstrated significant anti tumour activity and tolerability in advanced melanoma following PD-1 antibody treatment

treatment options post anti PD-L1/PD-1 failure are limited for melanoma patients. ipilimumab appears to have similar efficacy in front line vs second line and improves outcomes when combined with PD1, although it greatly increases toxicity and finally responses with low dose ipi may be maintained, decreasing toxicity. this prospective clinical trial initially enrolled 35 patients with advanced melanoma, no prior CTLA4 antibodies for metastatic disease, and who had progressed on PD-1 antibodies as immediate prior therapy [or a non-CTLA4 antibody combination]. the primary endpoint was response rate [RR] with secondary endpoints of safety, progression free survival, overall survival, as well as exploratory biomarkers of immune response. most patients had a prior PD-1 antibody on its own with14% having investigational PD-1 combinations, and 7% of patients receiving prior BRAF-targeted therapy, none of which was in the adjuvant setting. RR was was 27% - higher than the 15% in historical controls with ipi alone. a median duration of response of 18.5 months was observed. not all responses were sustained. median progression free survival was five months. median overall survival was 24.7 months. clinical trial information NCT02743819.

ipilimumab alone or in combination with anti-PD-1in patients with metastatic melanoma resistant to PD1 monotherapy abstract 10005

predictive models of response and survival will help forecast patient outcomes with ipi + PD1 after progressing on PD1 monotherapy

PD1 induces long term responses in approximately 30% of metastatic melanoma patients, however 2/3 are resistant [innate or acquired] and will require further treatment. a subset of these patients will benefit from IPI or IPI+PD1, but are yet to be identified.

this study retrospectively evaluated 330 patients with metastatic melanoma who were resistant to PD-1 and subsequently treated with ipilimumab alone [161; 49%] or in combination with PD-1 [169; 51%] to assess response rate, survival, and predictors of both.

in patients resistant to PD1, ipi combined with PD1 resulted in a higher response rate [32%] and longer PFS [25% at 12 months] and OS [58% at 12 months], yet similar high grade toxicity than ipi alone.

EFFECTIVE RECHALLENGE WITH CHECKPOINT INHIBITORS IN MELANOMA PATIENTS IS FEASIBLE EVEN FOR THOSE WITH A PRIOR HISTORY OF DISEASE PROGRESSION

overall survival and biomarker analysis of a phase Ib combination study of toripalimab, a humanized IgG4 mAb against programmed death-1 [PD-1] with axitinib in patients with metastatic mucosal melanoma abstract 10007

toripalimab with axitinib is a promising treatment regimen for metastatic mucosal melanoma-GEP scores may predict response

metastatic mucosal melanoma responds poorly to PD-1 blockade therapy in comparison with cutaneous melanoma. vascular endothelial growth factor [VEGF] is indicated to play an important immunosuppressive role in mucosal melanoma. combination of VEGF inhibition with PD-1 blockade might provide therapeutic opportunities. the study objective was to evaluate the safety and clinical efficacy of toripalimab combined with axitinib for the treatment of metastatic mucosal melanoma.

among 29 treatment naïve patients, 14 showed partial response and 11 had stable disease; the overall response rate was 48.3%. median progression free survival was 7.5 months; median overall survival was 20.7 months. treatment related adverse effects occurred in 97% of patients [39.4% were grade 3/4]. PD-L1 expression or tumour mutational burden [TMB] had no significant differences in responders versus non responders. in contrast, GEP showed a strong correlation with clinical response. clinical trial information NCT03086174

long term survival from pembrolizumab completion and pembro retreatment. phase III KEYNOTE-006 in advanced melanoma abstract 10013

pembro retreatment can provide additional clinical benefit in a majority of patients

five year follow up of the phase III KEYNOTE 006 study showed pembro improved OS vs ipilimumab in patients with advanced melanoma. three year OS rate from pembro completion for patients who completed two years of pembro was 93.8%. results with eight months of additional follow up were presented to inform clinical care.

OS at 36 months in the pembro group [103] was 100% among patients with complete response, 94.8% among patients with partial response, and 66.7% among patients with stable disease. 15 patients received a second course of pembro, best observable response [BOR] was 6 CR, 6 PR and 3 SD. the median time between pembro courses was 24.5 months with BOR on 2nd course 3 CR, 5 PR, 3 SD and 2 PD and two patients pending.

pembro improves the long term survival vs ipi in patients with advanced melanoma, with all patients who completed therapy in CR still alive at five years. retreatment with pembro at progression in patients who stopped at SD or better can provide additional clinical benefit in a majority of patients. clinical trial information NCT01866319

A SUBSET OF PATIENTS WHO INITIALLY RESPOND TO THERAPY WILL PROGRESS, LEAVING THE MAJORITY OF PATIENTS IN NEED OF AN EFFECTIVE SECOND LINE APPROACH

the IMPemBra trial, a phase II study comparing pembrolizumab with intermittent, short term dual MAPK pathway inhibition plus pembrolizumab in melanoma patients harbouring the BRAFV600 mutation abstract 10021

intermittent short time combination therapy enables therapy with MAPKi as a second line, and therefore warrants further investigation

this study evaluated the optimal duration of treatment with trametinib [MAPKi] plus dabrafenib [BRAFi] in combination with pembrolizumab [anti-PD-1] in BRAFV600 mutated melanoma patients. the study assessed the regimen relative to its safety, feasibility, and immune activating capacity.

treatment naïve patients were started on pembrolizumab and randomized at six weeks to continue pembro only [cohort 1], or to receive, in addition to pembro, dabrafenib + trametinib 2 x 1 week [cohort 2, 2 x 2 weeks [cohort 3], or continuously for six weeks [cohort 4].

pembro was given up to two years in all cohorts. grade 3/4 adverse events were observed in 12%, 12%, 50%, and 62% of patients in cohorts 1-4, respectively. ORR at week 18 was 62%, 75%, 75%, and 50% in cohorts 1-4, respectively. the median PFS in the pembro monotherapy group was 10.6 months compared with 27 months for the patients receiving pembro and short term dabrafenib + trametinib.

short term, intermittent dabrafenib + trametinib in combination with pembro was effective and more tolerable than continuous therapy with all three agents and warrants further investigation in a larger cohort. clinical trial information NCT02625337

THIS EVIDENCE INDICATES THAT MAPK TARGETED THERAPIES MAY SYNERGIZE WITH IMMUNE CELLS, THUS PROVIDING RATIONALE FOR THE DEVELOPMENT OF COMBINATION THERAPIES

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