save your skin FOUNDATION

LA FONDATION sauve ta peau

American Society of Clinical Oncology 2020 Virtual Meeting Report

A 2020 Report by Save Your Skin Foundation

Save Your Skin Foundation, June 2020

INTRODUCTION

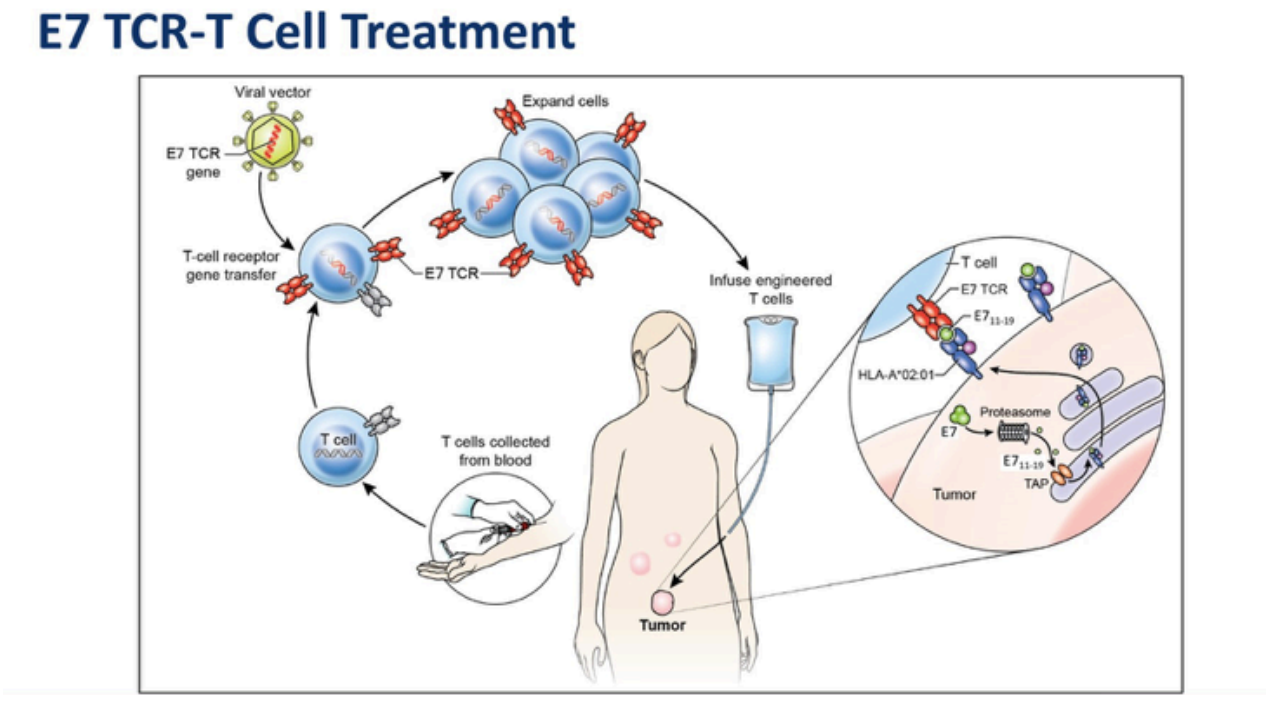
In 2020, the American Society of Clinical Oncology meeting was held online due to the COVID-19 pandemic. The meeting took place from May 29th-31st, with the last two days being devoted to online presentations. This report will be dedicated to the presentations that representatives from Save Your Skin Foundation remotely attended, with a focus on melanoma, innovative treatments, and survivorship. The information in this report is sourced directly, occasionally verbatim, from ASCO presentations and abstracts. If you require more information on an abstract, the clinical trial numbers (where available) are included for your reference.

TABLE OF CONTENTS

PANEL: HARNESSING IMMUNOTHERAPY WITH NOVEL APPROACHES BEYOND CHECKPOINT INHIBITORS

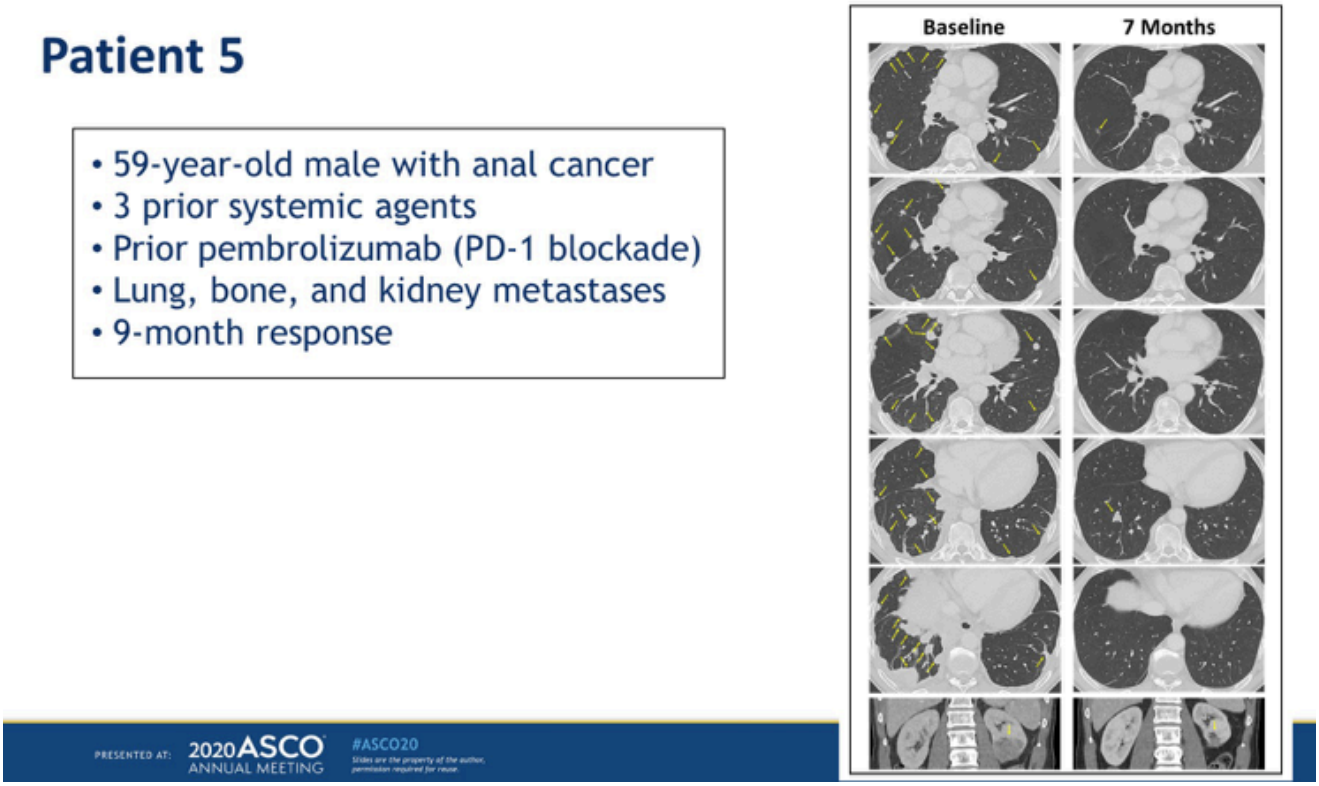
SAFETY AND CLINICAL ACTIVITY OF GENE-ENGINEERED T-CELL THERAPY TARGETING HPV-16 E7 FOR EPITHELIAL CANCERS BY SCOTT NORBERG (NATIONAL CANCER INSTITUTE AT THE NATIONAL INSTITUTES OF HEALTH)

Norberg's presentation focussed on abstract #101 (NCT02858310), which discusses a phase I clinical trial where patients with metastatic HPV-16+ epithelial cancers were treated with a one-time infusion of genetically-engineered T-cells that contained a T-cell receptor targeting an HLA-A*02:01-restricted epitope of HPV-16 E7 (E7 TCR-T cells), with a 3 + 3 dose escalation. For E7 TCR T-cell treatment, peripheral blood T-cells with an endogenous T-cell receptor (in grey in the image below) are obtained from a patient with metastatic cancer, which are then engineered to express a T-cell receptor. (red in image below). Patients were given a lymphocyte-depleting conditioning regimen before cell infusion, and a high-dose systemic aldesleukin after cell infusion. The trial involved twelve patients, who had previously been treated with between 3-7 anticancer agents.



(Slide from Norberg 2020)

Six patients demonstrated responses, including regression and elimination of tumours; these responses occurred in patients with vulvar, anal, head and neck, and cervical cancers. Four of these patients had previously received PD-1 based therapy. Responses lasted between 3-9 months, and sustained, high-level engrafting of E7 TCR-T cells in peripheral blood was observed and correlated with cell dose, but not critical response. One example of these results includes the slide below, the case of a 59-year-old man with anal cancer. Four tumours were resistant, and three of these demonstrated genetic defects in HLA-A*02:01 or BM2, and one demonstrated copy loss with deceased expression of antigens and interferon response molecules.



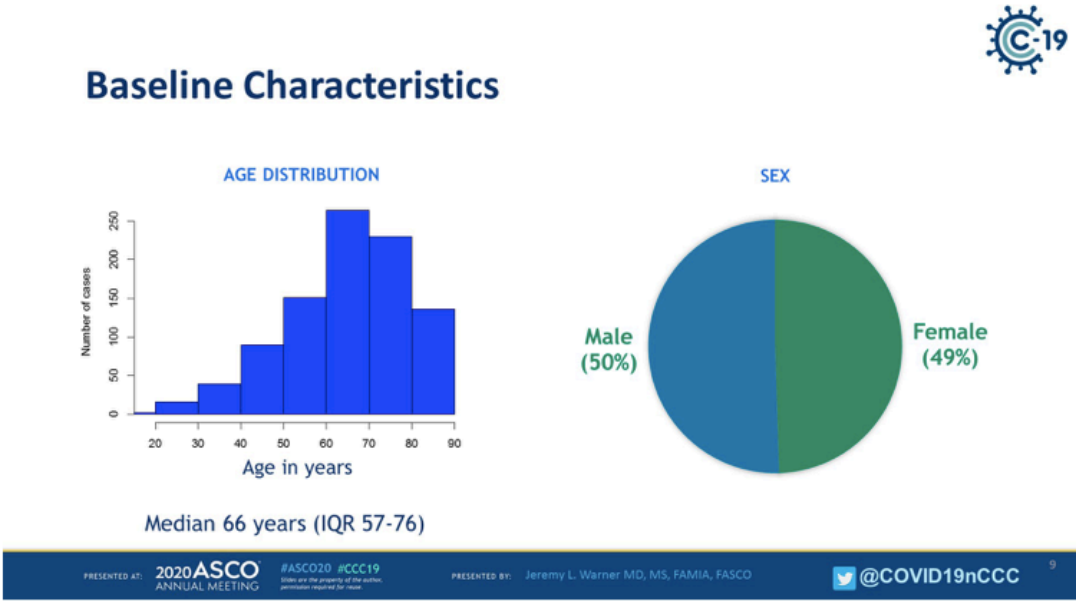
(Slide from Norberg 2020)

Overall, this abstract demonstrated that E7 TCR-T cells offer safe and clinical activity in the treatment of highlight refractory metastatic HPV-16+ cancers. Resistance to this treatment was linked to definitive genetic defects in the targeted peptide-HLA complex and to defects in antigen professing and interferon response.

PANEL: CANCER CARE IN THE TIME OF COVID: ASSESSING IMPACT AND FUTURE DIRECTIONS

CLINICAL IMPACT OF COVID-19 ON PATIENTS WITH CANCER: DATA FROM THE COVID-19 AND CANCER CONSORTIUM (CCC19) BY JEREMY LYLE WARNER, MD, MS, FASCO (VANDERBILT-INGRAM CANCER CENTER)

Warner presented on abstract # LBA110, a cohort study on the prevalence of COVID-19 in cancer patients that included patients with prior or active hematologist or invasive solid malignancies that were reported across community and academic sites. The study found that 1,018 cases of COVID-19 occurred in the study population within March and April 2020. The median age of these occurrences was 66 years old, and the most prevalent cancers were breast (20%) and prostate (16%). 82% of these patients had solid tumours. 43% of these patients were on anti-cancer treatment. At the time of data analysis, 26% of these patients required either hospitalization or mechanical ventilation, and 10.4% (106) patients had died. Factors associated with increased morality included male sex, age, ECOG performance status, history of being a smoker, active malignancy, and having received azithromycin and hydroxychloroquine. Cancer type and treatment were not independently associated with increased 30-day morality. Since the initial data analysis, the registry has accrued more than 2,000 cancer patients with COVID-19, and analysis of this cohort is impending.



(Slide from Warner 2020)

PANEL: DRUG DEVELOPMENT FOR RARE MUTATIONS: THE OPPORTUNITY TO UNITE AND CONQUER!

WHAT'S ENOUGH? REGULATORY CONSIDERATIONS BY STEVEN LEMERY, MD, MHS (U.S. FOOD AND DRUG ADMINISTRATION)

In this talk, Lemery, a medical oncologist within the Food and Drug Administration (FDA), discussing the regulatory process in the development of drugs for cancers with rare mutations. Lemery tackled this discussion in three parts: the challenges of researching drug effects in patients with rare mutations, how the FDA assesses clinical benefit in these scenarios, and risk benefit.

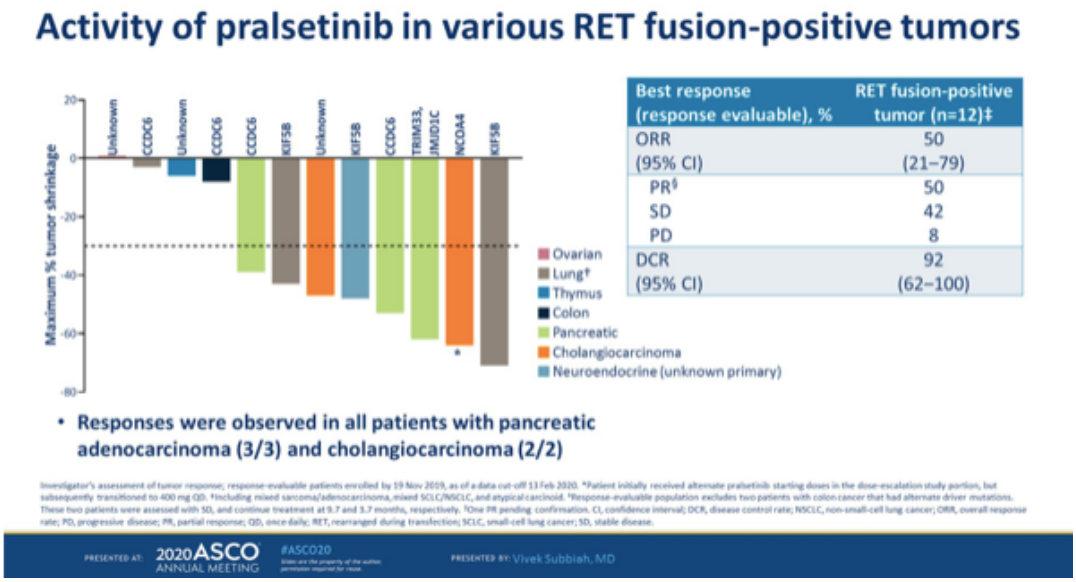
Lemery began by discussing the difficulties of developing drugs for patients with rare cancers. As Lemery notes, the financial cost of tests, and the availability of patient tissue samples to determine mutations, can be barriers, especially in the cases of patients with FGFR2, NTRK, or RET fusion-positive tumours. As Lemery notes, these are only testing barriers, and there are additional challenges for patients living in rural areas or financial hardships.

Lemery then discussed issues with determining clinical benefit. From Lemery's perspective, the requirement of overall survival as an endpoint for all drugs is prohibitive. For example, Lemery highlights the response rates of up to 60% following the treatment of patients with Merkell-cell carcinoma with either pembrolizumab or avelumab. However, relying on intermediate endpoints that are not directly related to survival can also present issues, as these endpoints might not correlate with survival in practice.

In conclusion, Lemery discussed issues surrounding risk benefit, and the question of how much data is required in rare mutation settings. As data is more difficult to gain for patients with mutations, it is also more challenging to discern whether a drug will meet the standard required for approval, that there is substantial evidence that the drug will have the claimed effect. This is related to another aforementioned dilemma in testing data, which is whether survival should be the only measure to designate the effectiveness of a drug. While not having this as an endpoint would risk uncertainty in terms of toxicity, it would also allow more drugs to access the market, which could help a population of patients. Finally, Lemery noted that while the FDA does not consider cost in approval decisions, this does not negate the issue of drug inaccessibility for financial reasons.

CLINICAL ACTIVITY OF THE RET INHIBITOR PRALSETINIB (BLU-667) IN PATIENTS WITH RET FUSION + SOLID TUMORS BY VIVEK SUBBIAH, MD (UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER)

Subbiah discussed abstract #109 (NCT03037385), which demonstrated the clinical activity of pralsetinib in RET fusion+ solid tumour types other than non-small cell lung cancer, in which pralsetinib has already proven to be successful. The ARROW study, which is being continued by this trial, consists of a phase 1 dose escalation followed by a phase 2 expansion in patients wth advanced RET-altered solid tumors, with primary objectives of overall response rates and safety.



(Slide from Subbiah 2020)

29 patients with metastatic solid tumor types (16 papillary thyroid cancers, 1 undifferentiated thyroid, 3 pancreatic, 3 colon, 6 other) bearing a RET infusion received pralsetinib. Responses were observed across multiple fusion genotypes; in the entire population, most treatment-related adverse affects were grade 1-2, and only 4% of patients discontinued due to treatment-related adverse events. Based on these results, pralsetinib demonstrated broad and durable antitumor activity across multiple advanced solid tumour types, regardless of RET fusion genotype, and was well tolerated. This study is still ongoing.

LOST IN THE WOODS? SEEKING NOVEL THERAPIES FROM THE PATIENT'S PERSPECTIVE BY MARK ANDREW LEWIS, MD (INTERMOUNTAIN HEALTHCARE)

The final presentation in this panel was given by Mark Lewis, who is not only a medical oncologist at Intermountain Healthcare but also a patient and patient advocate. Lewis structured his talk by discussing two advancements in targeted therapy for rare diseases, futibatinib and the FOLFOX chemotherapy regimen, while also recognizing that the data and jargon associated with these advancements may be overwhelming for patients. Lewis argues that this state of being overwhelmed by information is not uncommon for cancer patients, who often turn to Google, or clinicaltrials.gov, and sees a massive volume of unfamiliar information.

As examples, Lewis turned to the FOENIX-CCA2 study, a multi-centre, phase II study of futibatinib in patients with intrahepatic cholangiocarcinoma with FGFR2 gene fusions, wherein the study found that the treatment had a 37.3% objective response rate, lasting a median of 8.3 months, and the FOLFOX chemotherapy regimen, which saw a clinically meaningful reduction in risk of death for patients with colon cancer, and 15% increase in 6-month and 12-month survival rates. Returning to the patient search interface, Lewis noted that when he searched related terms (cholangiocarcinoma + FGFR + FDA) on clinicaltrials.gov, he received 21 results, which is much for palatable for a patient. However, Lewis notes, patients are much more likely to search Google before reaching clinicaltrials.gov, which can also allow patients (admittedly, less reliable) access to accurate information. Therefore, Lewis suggests that physicians should play a role as curator of search results for patients, and be open to helping patients understand the information they find— this can be especially useful when patients find clinically actionable information about their particular mutation, as they will be able to identify what is relevant to their situation. Overall, Lewis sought to demonstrate that patients and physicians are a team against disease, and that it would behoove physicians to treat their patients as such.

PANEL: CANCER PREVENTION, RISK REDUCTION, AND GENETICS

TARGETED THERAPY BASED ON GERMLINE ANALYSIS OF TUMOR-NORMAL SEQUENCING (MSK-IMPACT) IN A PAN-CANCER POPULATION BY ZSOFIA KINGA STADLER, MD (MEMORIAL SLOAN KETTERING CANCER CENTER)

Stadler presented on abstract #1500, which analysed the clinical utility of germline mutation profiling for targeted therapeutic intervention in pan-cancer patient populations. For this study, patients who received germline genetic testing via a next-generation sequencing panel (MSK-IMPACT) from 2015-2019 were identified, and patients with likely pathogenic or pathogenic germline alterations in genes with therapeutic targets had their records reviewed to asses possibilities for germline-targeted treatment in a clinical or research setting.

The team identified 2,043 patients (17.1% of considered population) who harboured pathogenic or pathogenic germline variants in cancer predisposition genes, including 777 (6.5%) genes with potentially targetable therapeutic implications, as outlined in the table below.

Gene(s) with potential targetable therapy	Drug Class	% of advanced cancer patients receiving targeted therapy
BRCA1, BRCA2	PARP-I	50.9% (165/324)
Lynch syndrome (*MLH1, MSH2, MSH6, PMS2, EPCAM*)	Checkpoint-inhibitors	58.3% (42/72) (irrespective of MSI) 67.4% (29/43) (MSI-High)
ATM	PARP-I	19.3% (17/88)
PALB2	PARP-I	41.7% (15/36)
RAD51C, RAD51D	PARP-I	36.8% (7/19)
RET	Tyrosine kinase inhibitor	60% (3/5)
TSC	mTOR inhibitor	0% (0/3)
PTCH1	Hedgehog-signaling inhibitor	33.3% (1/3)
ALK	ALK kinase inhibitor	0% (0/2)
EGFR	EGFR inhibitor	100% (1/1)
MET	MET kinase inhibitor	0% (0/1)

(Slide from Stadler 2020)

The results of Stadler's pan-cancer study suggest that 6.5% of patients had a targetable germline variant, which highlights the importance of germline analysis in advanced cancer patients in selection of treatments and clinical trial participation.

TUMOR/NORMAL GENOMIC PROFILING IN PATIENTS WITH METASTATIC SOLID TUMORS IDENTIFIES PATHOGENIC GERMLINE VARIANTS OF THERAPEUTIC IMPORTANCE BY ERIN FRANCES COBAIN, MD (UNIVERSITY OF MICHIGAN)

Cobain discussed abstract #1501, which tested next-generation sequencing of of paired tumor/normal samples can identify incidental pathogenic germline variants. The study took place from 2011-2018, wherein 1,015 patients received targeted exome and transcriptome sequencing of matched tumor and normal samples. Pathogenic germline variants that were associated with certain autosomal recessive conditions or increased cancer risk were reported to the treating oncologist, and received were conducted every three months to assess whether the identification of these pathogenic germline variants impacted treatment decision making.

The results determined that targeted next-generation sequencing of matched tumor and normal samples identified pathogenic germline variants in about 1 in 6 patients with metastatic solid tumors. Pathogenic germline variants with therapeutic benefits were found in patients with a variety of cancer types, allowing targeted therapies to have significant clinical benefit in these cases. Therefore, pathogenic germline variants in DNA repair genes should be considered in treatment decision-making for patients with metastatic solid tumour malignancies.

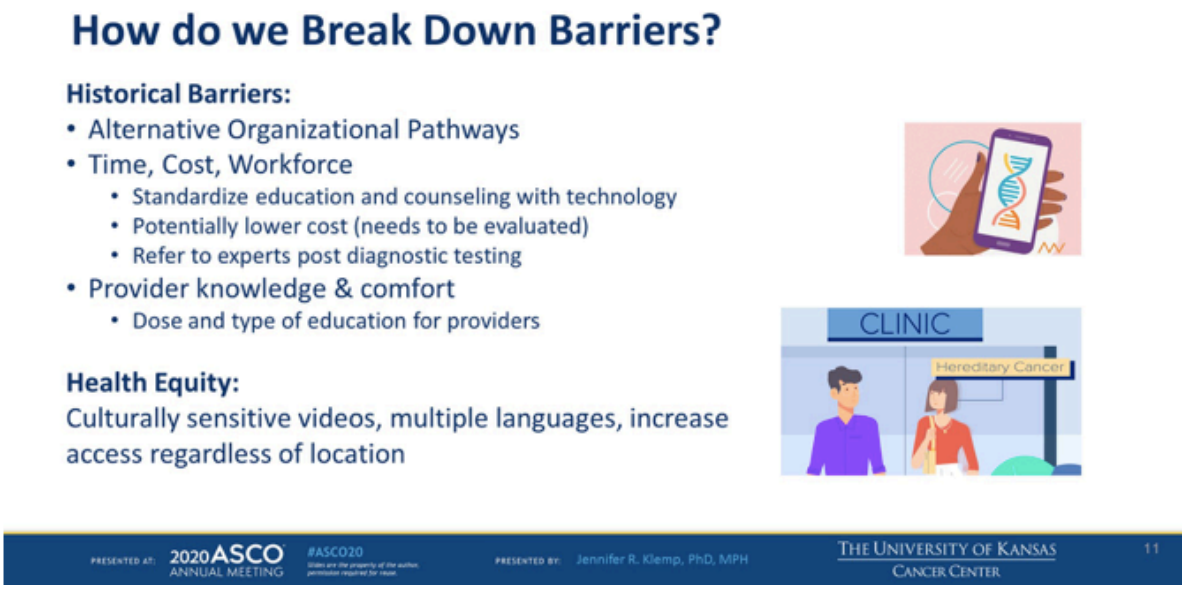
IT'S NOT WHAT YOU SAY, IT'S HOW YOU SAY IT: NEW GENETIC TESTING DELIVERY TITLES BY JENNIFER R. KLEMP, PHD, MPH, MA (DIVISION OF MEDICAL ONCOLOGY, UNIVERSITY OF KANSAS CANCER CENTER)

Klemp concluded this panel on cancer prevention, genetics, and risk reduction by further discussing the potential of genetic testing to cancer screenings and reduction of risk. Genetic testing, Klemp explains, would also be useful for identifying hereditary cancer risk; between just breast, ovarian, and prostate cancer, there are a potential for 75,000 patients to be identified with heredity cancer risk in 2020.

However, Klemp goes on to explain, there are still many barriers to testing access. Cost, time, and workforce availability (including professional training) have been consistently cited as problems with access to

genetic testing. Access disparities also exist in terms of race (African-Americans have lower testing rates), insurance coverage, and for patients in rural areas.

Klemp then discussed the study Magenta, a non-inferiority study with a control arm and three intervention arm, which evaluated how an online genetic educational video with or without genetic counselling worked in assessing cancer risk distress in patients with a personal or family history of breast and/or ovarian cancer. The study found that more patients completed the online training that had not also received telephone pre-test counselling, which suggests that some aspect of pre-test counselling affects patients undergoing the testing process. Klemp considered educational fatigue to be a possible factor. However, Klemp later states that this particular study was valuable by suggesting ways to incorporate technology into clinical pathways, which might provide educational opportunities that can be suited to patients' styles of learning. Online education platforms, such as the ones in this study, can be useful in both in-clinic and telehealth settings, however Klemp believes that more research needs to be done to discern the optimal way to deliver this education to patients.



(Slide from Klemp 2020)

PANEL: CARE DELIVERY AND REGULATORY POLICY

INTERVENTION COMBINING NURSE NAVIGATORS (NNS) AND A MOBILE APPLICATION VERSUS STANDARD OF CARE (SOC) IN CANCER PATIENTS (PTS) TREATED WITH ORAL ANTICANCER AGENTS (OAA): RESULTS OF CAPRI, A SINGLE-CENTER, RANDOMIZED PHASE III TRIAL BY OLIVIER MIR, MD, PHD, MPH (GUSTAVE ROUSSY CANCER INSTITUTE)

Mir presented Abstract #2000 (NCT02828462), which discussed CapRI, a randomized phase III trial that compared an intervention that combined nurse navigators and a mobile application, versus standard of care, in cancer patients treated with oral anticancer agents. The nurse navigators provided regular telephone followups to manage symptoms and assess toxicities, adherence and supportive care needs, in addition to connecting with patients through a mobile application, for a period of six months. The primary endpoint for the study was relative dose intensity, with secondary endpoints of toxicity, adherence, response and survival, end-of-life support, quality of life, and economic usage of healthcare resources.

The results found that the CapRI intervention improved relative dose intensity, hospitalizations and their duration, treatment-related grade>3 toxicities, and patient experience. This type of remote care, Mir suggests, should be a new standard for receiving oral anticancer agents.

CHEMOTHERAPY REMOTE CARE MONITORING PROGRAM (CTCMP): INTEGRATION OF AN SMS TEXT PATIENT-REPORTED OUTCOME (PRO) IN THE ELECTRONIC HEALTH RECORD (EHR) TO IDENTIFY PATIENTS NEEDING PHARMACIST INTERVENTION FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING BY SHANNON HOUGH, PHARMD, BCOP (UNIVERSITY OF MICHIGAN, ANN ARBOR)

Hough presented Abstract #2001, which initiated the chemotherapy remote care monitoring program (CTCMP) to identify and intervene in patients experiencing chemotherapy-induced nausea and vomiting. Patients that were receiving highly emetogenic chemotherapy were identified and enrolled in the CTCMP, and then received a daily text message survey for 7 days after their treatment. Responses to questions regarding nausea that were above a set threshold triggered a message to the patient's pharmacist team for intervention.

Of the patients enrolled in the study, 51.7% were taking the chemotherapy curatively, and 48.3% palliatively. The text response rate to the survey was 94%, and since the implementation of the CTCMP,

hospitalization, urgent care use, and emergency department use has decreased, especially when considering utilization of these services for nausea-related diagnoses. Demonstrably, patient engagement in the CTCMP reduced health care usage for patient nausea.

	BEFORE CRCMP (n=3504 doses)	AFTER CRCMP (n=2244 doses)	p value
Admissions (ED/IP/OBS)	124	80	0.958
Nausea-Related Admissions	22	7	0.1
Urgent Care	110	38	0.001
Nausea-Related Urgent Care	23	7	0.077
Total visits	234	118	0.029
Total Visits: Nausea-Related	45	14	0.015

(Slide from Hough 2020)

HOME-BASED MANAGEMENT OF CANCER PATIENTS (CPS) EXPERIENCING TOXICITIES WHILE ON ANTICANCER TREATMENTS: THE IMPACT OF A NURSE-LED TELEPHONE TRIAGE (NTT) BY LORENZO CALVETTI, MD (DEPARTMENT OF ONCOLOGY, SAN BARTOLO GENERAL HOSPITAL)

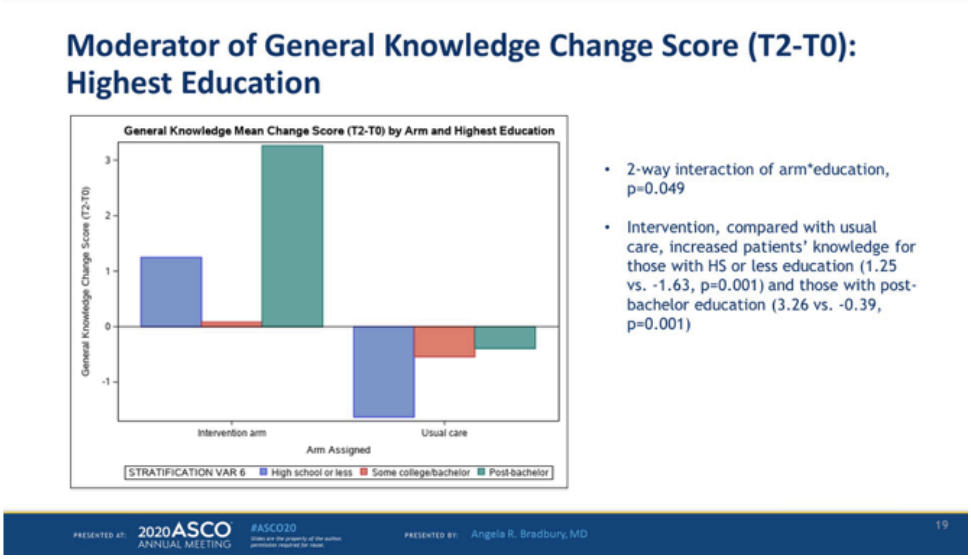
Calvetti presented Abstract #2002, which studied the affects of a nurse telephone triage (NTT) in reducing hospitalization of cancer patients. For the study, cancer patients at Calvetti's home institute, the San Bartolo General Hospital, were told to contact the NTT in case of treatment-related adverse affects. The triage nurses were trained oncological nurses, and took actions appropriate to the adverse affects. The primary endpoint of this study was to compare the hospitalization of cancer patients on anti-cancer medication after the introduction of the NTT, versus the 2017-2018 period.

During the study period, September 2018-September 2019, cancer patients reported 581 adverse events over 429 consultations with a triage nurse; 109 cancer patients were hospitalized for these adverse affects. In the 2017-2018 period, 138 were hospitalized, showing a reduction from 14.7% to 10.1%. These results demonstrate that successful implementations of the NTT system may reduce rates of hospitalization due to cancer treatment-related adverse events.

RANDOMIZED TRIAL OF WEB-BASED GENETIC EDUCATION VERSUS USUAL CARE IN ADVANCED CANCER PATIENTS UNDERGOING TUMOR GENETIC TESTING: RESULTS FROM THE ECOG-ACRIB NCI COMMUNITY ONCOLOGY RESEARCH PROGRAM (NCORP; EAQ152) COMET TRIAL BY ANGELA R. BRADBURY, MD (UNIVERSITY OF PENNSYLVANIA)

Bradbury presented Abstract #2008 (NCT02823652), which tested a web-based intervention to increase genetic knowledge and decrease stress in advanced cancer patients who were undergoing tumour genetic testing. In this study, 594 patients were randomized to web-intervention or usual care, prior to receiving their tumour genetic test results. The primary outcomes for the study were depression, anxiety, genetic knowledge, and cancer-specific distress; the secondary outcomes included regret, disappointment, and satisfaction.

The results demonstrated that patients who had been randomized to the web-based intervention had better knowledge than those who had been given usual care. However, no differences were reported in terms of depression, anxiety, or cancer-specific distress between the two cohorts. Bradbury et al. concluded that web-based education increases patient knowledge of tumour genetic testing, however this web-based education does not remarkably reduce distress, and cancer-related distress. Future refinements to the web-based education platform could serve to better address low-literacy groups.

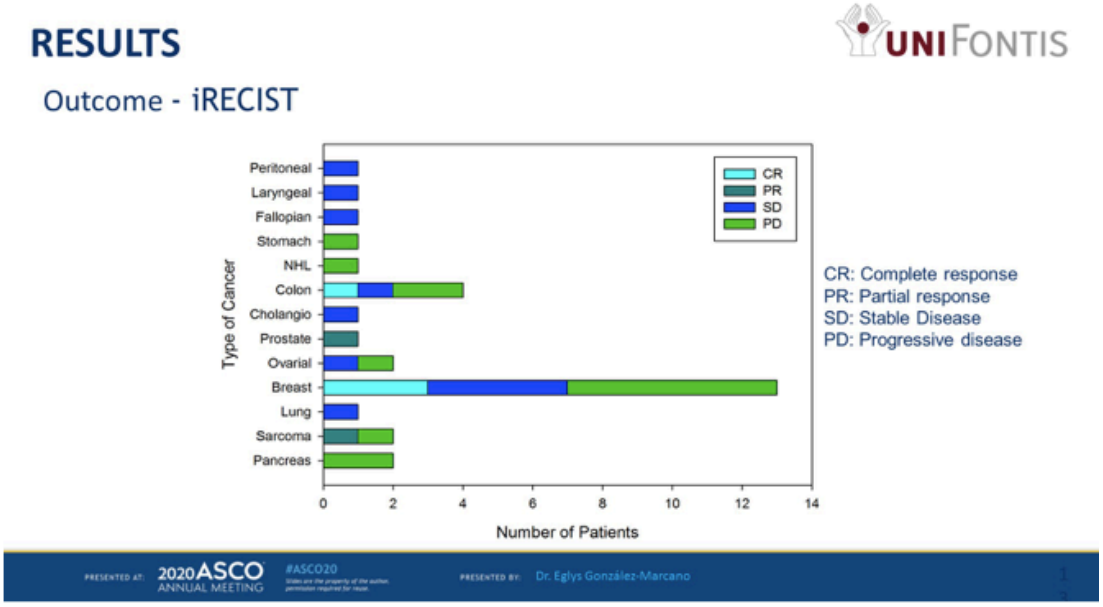


(Slide from Bradbury 2020)

PANEL: DEVELOPMENTAL THERAPEUTICS—IMMUNOTHERAPY

PILOT STUDY ON OUTCOME AND ANTITUMOR EFFICACY OF AN AUTOLOGOUS CANCER CELL VACCINE APPLIED IN PATIENTS WITH ADVANCED SOLID TUMORS BY EGLYS GONZALEZ MARCANO, PHD (UNIFONTIS)

Marcano presented Abstract #3000, a pilot study that evaluated the clinical relevance and outcomes of autologous vaccine immunotherapy as a treatment for different types of cancer. Autologous vaccines are made with the patient's own tumour cells, which are processed in vitro, eliciting a cytotoxic T-lymphocytic immune response against tumour cell antigens. For the study, 31 patients with advanced solid tumours, who had not received standard treatments, were treated with six intradermal doses of the vaccine over two months. Two of these patients suffered from pancreatic cancer, two from sarcoma, one from lung cancer, thirteen from breast cancer, two from ovarian cancer, one from prostate cancer, one from cholangiocarcinoma, four from colorectal cancer, one from non-Hodgkin lymphoma, one from gastric cancer, one from laryngeal and hypopharyngeal cancer, one from fallopian tube cancer, one from peritoneal cancer. Results were measured in metric response and tumour markers, where available.



(Slide from Marcano 2020)

The results confirmed that autologous vaccine therapy had an anti-tumor response in the trial patients, with minimal side effects (occasional redness around the injection area, and inflammation of the tumour area in one case). Marcano suggested that further controlled clinical study should be performed in order to obtain more detailed data on this treatment method.

NOVEL APPROACHES TO OPTIMIZING IMMUNE CHECKPOINT INHIBITORS BY SANDIP PRAVIN PATEL, MD (UNIVERSITY OF CALIFORNIA, SAN DIEGO)

Patel's presentation discussed Abstracts #3003, #3004, and #3005, all of which focussed on new immunotherapy combinations and strategies to make immunotherapy more effective. Patel began by noting that in any novel immunotherapy trial, it is imperative to ascertain the tumour types that are being treated, what the patient population has been previously treated with, and what their responses were to this treatment, the history of the treatment plan being tested, and the biomarker selection of the patients in the study, the consistency of which can be essential in the success of clinical trials.

Moving into discussion of Abstract #3003 (Goldman et al.), which was an exploration of MEDIO562 (an OX40 agonist), in combination with either durvalumab (an anti- PD-L1 agent) or tremelimumab (an anti-CTLA-4 agent) in patients with advanced solid tumours. This was a phase I study across multiple tumour types, though the majority had cervical cancer. Six patients saw responses from MEDIO562 + durvalumab, with an especially high percentage in the cervical cancer patients, while no results were seen with the combination of MEDIO562 + tremelimumab. Therefore, the response to MEDIO562 + durvalumab was higher than expected, but still requires further validation. This finding is, Patel suggests, consistent with other research that has been conducted on this combination.

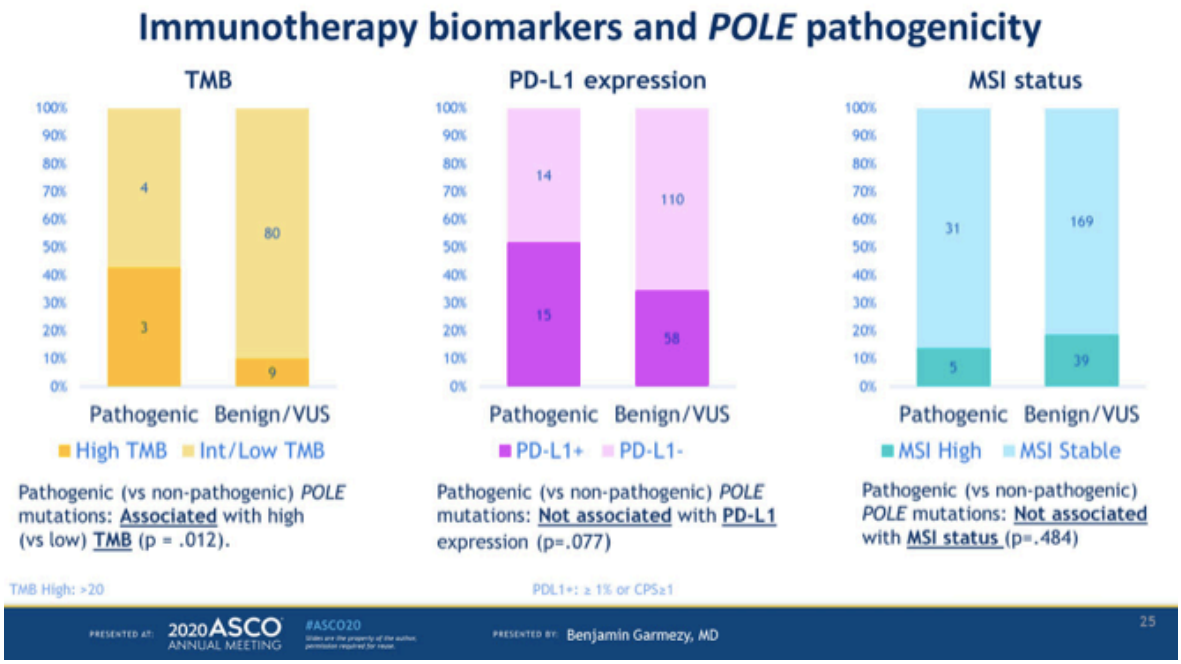
Patel moved on to discuss Abstract #3004 (Luke et al.), a phase I study of MGD013, a bispecific DART molecule-binding PD-1 and LAG-3 in patients with metastatic or unresectable neoplasms. As T-cells undergo exhaustion, receptors such as PD-1 and LAG-3 are upregulated, making the DART protein particularly effective in binding PD-1 and LAG-3 receptors. The trial treatment shows no emergent toxicities or safety alarms. Patel notes that this study raises the question of a combination anti-HER2 antibody and a PD-1 LAG-3 DART, which would maximize NK-cell-dependent killing in solid tumours.

Patel concluded by revisiting Abstract #3005 (Thistlethwaite et al.), a CX-072 study, a PD-L1 probody therapeutic, in combination with ipilimumab or as a single agent. This was a phase I trial which tested CX-072 as a monotherapy or combination in a variety of tumour types, and a phase II monotherapy expansion. In the phase I dose escalation, patients being treated with the combination, there was activity, as seen below, and fewer immune-related adverse events. The results also suggested new possibilities for CX-072 as a combination therapy, with further validation.

CORRELATION OF PATHOGENIC POLE MUTATION WITH CLINICAL BENEFIT TO IMMUNE CHECKPOINT INHIBITOR THERAPY BY BENJAMIN GARMEZY, MD (THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER)

Garmezy discussed Abstract #3008, which analyzed patients with advanced cancers and DNA polymerase epsilon mutations (POLE), which can induce DNA replication errors, increasing neoantigen load, which might enhance clinical benefit to immune checkpoint inhibitors. The study used targeted exome sequencing through CLIA-certified next generation sequencing assays to identify patients with POLE-aberrant tumours and their co-occuring mutations. Patients from a variety of cancer types were included, with melanoma making up 10.2% of the patients tested. 12, 947 patients participated, with 448 having a POLE mutation or variation.

The results showed a clinical benefit rate of 53.8%, with the pathogenic status of POLE mutation being associated with this clinical benefit. Therefore, the study demonstrated that pathogenic POLE mutations have clinical benefit to immune checkpoint inhibitor therapy, with more studies suggested to investigate POLE mutations as a predictive biomarker.



(Slide from Garmezy 2020)

PANEL: DEVELOPMENTAL THERAPEUTICS—MOLECULARLY TARGETED AGENTS AND TUMOR BIOLOGY

CX-2029, A PROBODY DRUG CONJUGATE TARGETING CD71 (TRANSFERRIN RECEPTOR): RESULTS FROM A FIRST-IN-HUMAN STUDY (PROCLAIM-CX-2029) IN PATIENTS WITH ADVANCED CANCER BY MELISSA LYNNE JOHNSON, MD (SARAH CANNON RESEARCH INSTITUTE, NASHVILLE, TN)

Johnson presented Abstract #3502 (NCT03543813), which tested CX-2029, a PROBODY drug conjugate of a microtubule inhibitor, against CD71. CD71 is highly expressed on normal cells, and are marked antibody drug conjugates, and therefore restrict target engagement to tumours. This study has preliminary results, collected from a phase 1/2 first-in-human study of PDC CX-2029 in advanced solid tumours, with 34 patients in escalating dose cohorts.Treatments were given via IV every 21 days. Endpoints for the study included evaluation of the maximum tolerable dose, antitumour activity, safety, and potential biomarkers. This study is particularly notable, as one of the participants was fighting ocular melanoma.

The most common treatment-related adverse event was injection-related, followed by anemia (56%), fatigue (24%), nausea (24%), neutropenia (21%), and leukopenia (12%), overall reducing toxicity for this target, and producing evidence of anti-tumour activity. The dose-escalation for this trial continues.

RESULTS FROM A PHASE I, OPEN-LABEL STUDY OF CERALASERTIB (AZD6738), A NOVEL DNA DAMAGE REPAIR AGENT, IN COMBINATION WITH WEEKLY PACLITAXEL IN REFRACTORY CANCER (NCT02630199) BY JEEYUN LEE, MD (SAMSUNG MEDICAL CENTER)

Lee presented Abstract #3503 (NCT02630199), which was a study of the effects of AZD6738, an oral inhibitor of the serine/threonine protein kinase Ataxia Telangiectasia and Rad3 Related (ATR), an apical kinase that has a critical role in DNA-damage response. ATR can lead to double strand breaks during DNA replication If left unchecked. For this study, 58 patients, including 34 melanoma patients, with advanced solid tumours were given AZD6738 in combination with a fixed dose of paclitaxel, with dosage escalating in 28-day cycles. The trial aimed to evaluate pharmacodynamics, maximum tolerable dose, safety, and pharmacokinetics. In the melanoma patient

cohort, 1 complete response was seen, and 10 partial responses. Toxicities included nausea (26%), anorexia (26%), anemia (19%), and leukopenia (19%).

The study results concluded that AZD6738 can safely be combined with paclitaxel, and the organizers have suggested a phase II dose schedule. This combination displayed promising anti-tumour activity and durable responses, especially in melanoma patients who had failed anti-PD1 therapy.

PHASE I STUDY OF 9-ING-41, A SMALL MOLECULE SELECTIVE GLYCOGEN SYNTHASE KINASE-3 BETA (GSK-3B) INHIBITOR, AS A SINGLE AGENCY AND COMBINED WITH CHEMOTHERAPY, IN PATIENTS WITH REFRACTORY TUMOURS BY BENEDITO A. CARNEIRO MD, MS (BROWN UNIVERSITY)

Carneiro presented Abstract #3507 (NCT03678883), which tested 9-ING-41, a GSK-3β (a serine/threonine kinase) inhibitor that has exhibited broad-spectrum pre-clinical antitumour activity, including chemotherapy-resistant models. Overexpression of GSK-3β can result in aggressive tumour growth, advanced stage malignancies, and chemotherapy resistance. This study evaluates the efficacy, safety, and pharmacokinetics of 9-ING-41 monotherapy in combination with chemotherapy in patients with refractory malignancies. 9-ING-41 is given via IV as a single agent, or combined with gemcitabine/nab-paclitaxel, gemcitabine, doxorubicin, carboplatin/paclitaxel, irinotecan, or lomustine in patients previously treated with chemotherapy.

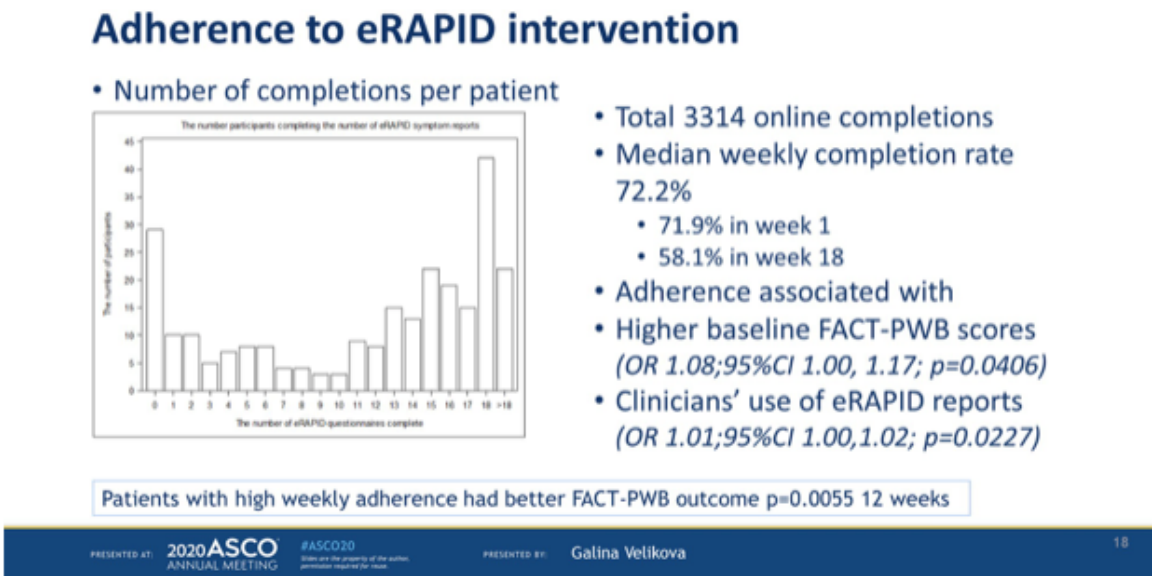
101 patients were enrolled in the trial, including 7 with melanoma. 31% of patients, including 2 melanoma patients, had stable disease as their best response. The results suggest that 9-ING-41 is well tolerated with significant antitumour activity as monotherapy, and in combination with chemotherapy. Enrolment in the study is still ongoing.

PANEL: HEALTH SERVICES RESEARCH AND QUALITY IMPROVEMENT

PHASE III RANDOMIZED CONTROLLED TRIAL OF ERAPID (ELECTRONIC PATIENT SELF-REPORTING OF ADVERSE-EVENTS: PATIENT INFORMATION AND ADVICE)—AN EHEALTH INTERVENTION DURING CHEMOTHERAPY BY GALINA VELIKOVA, PHD (LEEDS INSTITUTE OF MEDICAL RESEARCH AT ST JAMES'S)

Velikova presented Abstract #7002 (ISRCTN88520246), which evaluated eRAPID, an online platform for patients to report their symptoms. eRAPID provides advice to patients dependant on their symptoms and symptom severity, including alerts for hospital visits. Ostensibly, eRAPID and platforms like it can improve symptom management, survival, and quality of life. This study consisted of a two-arm parallel group, with 1, 484 patients overall, wherein one group reported their symptoms online to eRAPID once per week.

While the two arms saw no difference in chemotherapy delivery or metastatic disease, the immediate advice that came with online monitoring improved symptom control in the early stages of chemotherapy. The improvements in patient self-efficacy and education that the online platform presented demonstrate that it is a useful tool for patient care in the case of adjuvant chemotherapy.



(Slide from Velikova 2020)

U.S. TRENDS AND RACIAL/ETHNIC DISPARITIES IN OPIOID ACCESS AMONG PATIENTS WITH POOR PROGNOSIS CANCER AT THE END OF LIFE (EOL) BY ANDREA CATHERINE ENZINGER, MD (DANA-FARBER CANCER INSTITUTE)*

Enzinger presented Abstract #7005, which considered the access disparities for racial and ethnic minorities in the U.S. medical system, particularly in the cases of pain-related emergency department visits and opioid access in advanced and end-of-life cancer patients. The study considered a 20% random sample of Medicare Fee-for-Service beneficiaries, which consisted of 243, 124 patients with poor prognosis cancers, who died between 2007-2016. Researchers examined trends for the overall cohort and by race (categorized as white, black, and other), including geographical adjustments were made for patient demographic and clinical characteristics, opioid supply, year, and state. The trends analyzed were outpatient opioid prescription fills and pain-related emergency department visits near end-of-life.

The results noticed overall decreases in opioid prescription fills overall during between 2007-2016, with larger decreases in black patients (prescription fills fell 39.3% to 29.8% for black patients, versus 42.2% to 36.5% for white patients; prescription fills for long-acting opioids near end-of-life fell from 15% to 9% in black patients, versus 17% to 12% overall). In the adjusted statistics, black patients were less likely to receive end-of-life opioids, and on average received a dose of 10 fewer morphine milligram equivalents than white patients. Black patients, and patients of over races, were more likely than white patients to have pain-related emergency department visits near death. The results suggest that despite U.S. effort to mitigate the affect of opioid regulations on cancer patients, there are still significant racial and ethnic disparities in opioid access.

*While the Medicare Fee-for-Service model analyzed here is particularly American, economic, demographic, and language barriers to medical services are problems for Canadian Indigenous, homeless, and immigrant populations— these marginalized groups are of urgent importance when considering issues of access to prohibitively expensive treatments, patient education, and access to clinical trials.

PANEL: MELANOMA/SKIN CANCERS

PEMBROLIZUMAB VERSUS PLACEBO AFTER COMPLETE RESECTION OF HIGH-RISK STAGE III MELANOMA: NEW RECURRENCE-FREE SURVIVAL RESULTS FROM THE EORTC 1325-MG/KEYNOTE 054 DOUBLE-BLINDED PHASE III TRIAL AT THREE-YEAR MEDIAN FOLLOW-UP BY ALEXANDER M. EGGERMONT, MD, PHD, FASCO, BA (PRINCESS MÁXIMA CENTER, UTRECHT)

Eggermont presented Abstract #10000 (NCT02362594), a phase III double-blind EORTC 1325/ KEYNOTE-054 trial, which evaluated Pembrolizumab versus placebo in patients with with high-risk resected stage III melanoma. The results led to the approval of Pembrolizumab adjuvant treatment by the EMA and FDA, after 351 recurrence-free survival cases. The study included 1, 019 patients, who were given Pembrolizumab until unacceptable toxicity or disease recurrence. The two endpoints were relapse free survival in patients with PD-L-1 positive tumours, and overall patient population.

		3-yr RFS rate		Stratified by stage at randomization	
	N pts	Pembrolizumab	Placebo	HR	CI (HR)*
Overall population	1019	64%	44%	0.56	0.47-0.68
PD-L1 positive	853	65%	46%	0.57	0.43-0.74
PD-L1 negative	116	57%	33%	0.45	0.23-0.90
Stage IIIA	152	81%	66%	0.50	0.22-1.16
Stage IIIB	472	66%	47%	0.56	0.39-0.81
Stage IIIC	395	54%	32%	0.57	0.40-0.81
BRAF-mutated	440	62%	37%	0.51	0.36-0.73
BRAF-WT	448	62%	47%	0.66	0.46-0.95

(Image from Abstract #10000)

The results (above) demonstrated that Pembrolizumab prolonged the relapse free survival in both the general patient group and those with PD-L1 positive tumours, and particularly patients with BRAF-V600 E/ mutation status. The results demonstrate that Pembrolizumab provided a sustained improvement in relapse free survival, including in patients with high-risk resected stage II| melanoma.

LONG-TERM BENEFIT OF ADJUVANT DABRAFENIB + TRAMETINIB (D+T) IN PATIENTS (PTS) WITH RESECTED STAGE III *BRAF* V600–MUTANT MELANOMA: FIVE-YEAR ANALYSIS OF COMBI-AD BY AXEL HAUSCHILD, MD (UNIVERSITY HOSPITAL SCHLESWIG-HOLSTEIN)

Hauschild presented Abstract #10001 (NCT01682083), a five-year analysis of COMBI-AD, which consisted of 12 month treatment with dabrafenib + trametinib, in patients with resected stage ||| BRAF V600E/K-mutant melanoma. Previous results have demonstrated a significant relapse-free survival (RFS) benefit, with a three-year RFS rate of 58%. The primary endpoint is RFS, with secondary endpoints of distant metastasis-free survival and overall survival. Here, Hauschild et al. report data from a 5-year analysis of this treatment combination, including an updated cure rate model.

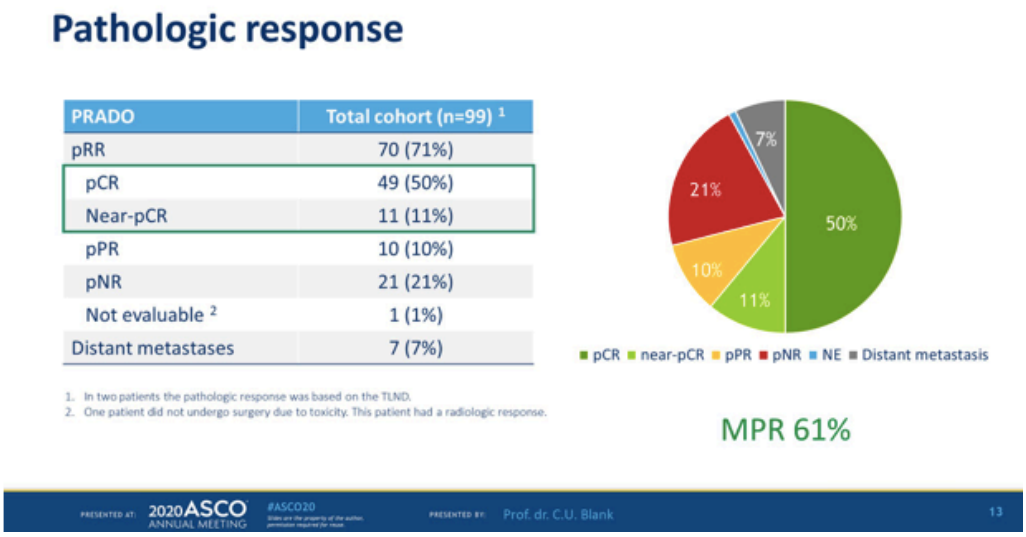
As anticipated by the COMBI-AD cure rate model, the 4- and 5- year RFS rates for this combination were 55% and 52% respectively, versus 38% and 32% respectively for the placebo. Therefore, this five-year analysis continues to demonstrate the long-term clinical benefits of adjuvant dabrafenib + trametinib for patients with resected stage III BRAF V600E/K-mutant melanoma.

FIRST SAFETY AND EFFICACY RESULTS OF PRADO: A PHASE II STUDY OF PERSONALIZED RESPONSE-DRIVEN SURGERY AND ADJUVANT THERAPY AFTER NEOADJUVANT IPILIMUMAB (IPI) AND NIVOLUMAB (NIVO) IN RESECTABLE STAGE III MELANOMA BY CHRISTIAN U. BLANK, MD, PHD (NETHERLANDS CANCER INSTITUTE)

Blank presented Abstract #10002 (NCT02977052), which discussed PRADO, a phase II study of personalized surgery and adjuvant therapy after the combination of neoadjuvant ipilimumab + nivolumab in patients with resectable stage III melanoma. PRADO was an extension cohort of the OpACIN-neo study, which tested 3 dosing options for neoadjuvant IPI+NIVO, ultimately identifying 2 cycles of the combination as the most favourable, with a pathologic response rate of 77%. In a 17.6 month median follow-up, 2% of the patients who

had shown pathologic response, versus 62% of the non-responders, experienced a relapse. The results suggested that additional adjuvant therapy might improve the outcome for patients that initially did not respond.

This hypothesis was tested by PRADO, a 99-patient study which tested response-driven subsequent therapy and the pathologic response and safety of neoadjuvant I1N3. Patients with clinical stage III melanoma received two cycles of neoadjuvant I1N3 after marker places in the index node. Patients that received major pathologic response did not receive therapeutic lymph node dissection, while patients who demonstrated lesser or no response underwent therapeutic lymph node resection and, in some cases, received additional adjuvant nivolilumab or targeted therapy. The primary endpoints for this study were relapse-free survival and pathologic response in the index node.



(Slide from Blank 2020)

The results of PRADO suggest that neoajduvant I1N3 treatment induced a high pathologic response rate, with tolerable levels of toxicity. A major subset of patients did not receive therapeutic lymph node dissection, and longer follow-up is needed to establish safety and relapse-free survival when therapeutic lymph node dissection is omitted in patients with major pathologic response.

A PHASE II STUDY TO EVALUATE THE NEED FOR > TWO DOSES OF NIVOLUMAB + IPILIMUMAB COMBINATION (COMBO) IMMUNOTHERAPY BY MICHAEL A. POSTOW, MD (MEMORIAL SLOAN KETTERING CANCER CENTER)

Postow discussed Abstract #10003 (NCT03122522), a phase II study which evaluated the utility of more than two doses of nivolumab + ipilimumab combination immunotherapy in patients with unresectable stage III/IV melanoma, as previous data demonstrates that patients can still have durable benefit even when they are given fewer than the standard 4 doses of the nivo + ipi comobination due to toxicity. In this trial, 60 patients with unresectable stage III/IV melanoma received two doses of the combination, followed by a CT scan at week 6. Patients who demonstrated favourable anti-tumour effect after the two doses transitioned to maintenance nivolimumab, while the remaining patients received the standard four doses of the combination.

41, or 68% of patients, received only the two doses of the combination. These results suggest that the first two doses of the combination are the seed for the combination's response efficacy and toxicity, and that imaging at week 6 may help determine whether patients will or will not respond to treatment beyond the second dose. Future randomized studies are planned to evaluate whether efficacy can be maintained with reduced toxicity after one dose of the combination.

SIGNIFICANT ANTITUMOR ACTIVITY FOR LOW-DOSE IPILIMUMAB (IPI) WITH PEMBROLIZUMAB (PEMBRO) IMMEDIATELY FOLLOWING PROGRESSION ON PD1 AB IN MELANOMA (MEL) IN A PHASE II TRIAL BY DANIEL OLSON, MD (UNIVERSITY OF CHICAGO COMPREHENSIVE CANCER CENTER)

Olson presented Abstract #10004 (NCT02743819), which reported the results of the first clinical trial to evaluate ipilimumab + pembrolizumab following progression with PD1 antibodies. The trial included 70 patients with advanced melanoma who had progressed on PD1 antibodies as prior therapy. These patients received pembrolizumab + ipilimumab for 4 doses, before receiving pembrolizumab for up to two years. The endpoint was response rate by immune-related response evaluation criteria in solid tumours (irRECIST).

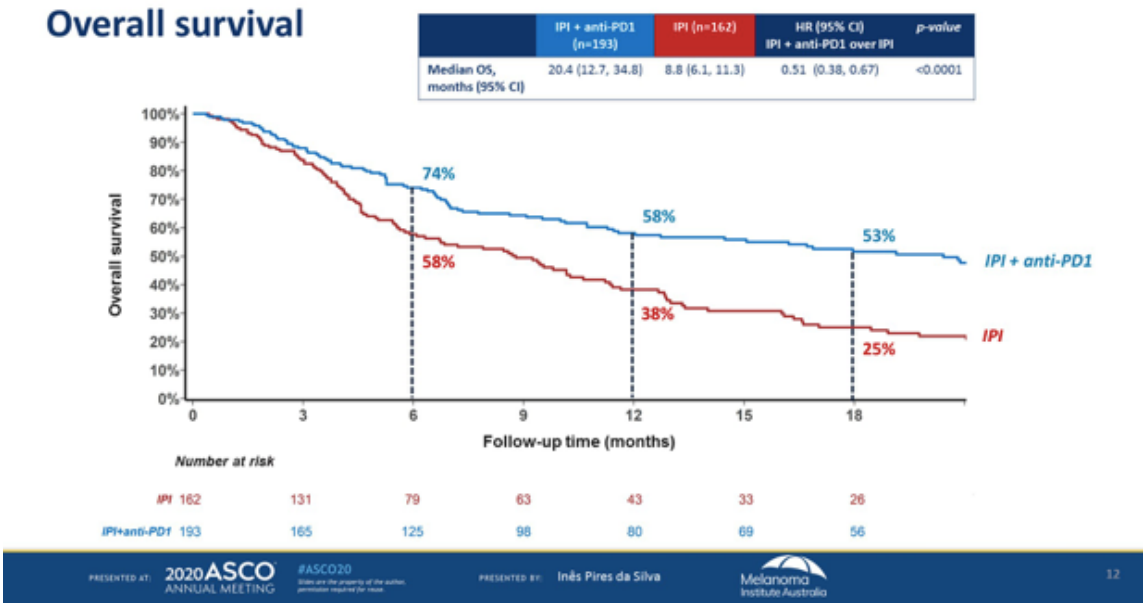
The irRECIST response rate to this combination was 25% for evaluable patients and 24% for enrolled patients; the median progression-free survival was 4.7 months, with the progression-free survival rate at 6 months being 45%. This study, which was the largest prospective study of the ipilimumab + pembrolizumab combination, demonstrates significant antitumour activity and tolerability in melanoma for patients post-PD1 antibody.

IPILIMUMAB (IPI) ALONE OR IN COMBINATION WITH ANTI-PD-1 (IPI+PD1) IN PATIENTS (PTS) WITH METASTATIC MELANOMA (MM) RESISTANT TO PD1 MONOTHERAPY BY INES PIRES DA SILVA, MD (MELANOMA INSTITUTE AUSTRALIA)

Da Silva discussed Abstract #10005, which aimed to determine survival and response rate for metastatic melanoma patients to ipilimumab with/without PD1 antibodies after PD1 progression, and to identify clinical predictors of survival and response to ipilimumab with/without PD1 antibodies. The study included 330 metastatic melanoma patients resistant to PD1 antibodies, with a median progression time of 2.9 months.

88% of the 330 patients received ipilimumab + PD1 as their adjuvant treatment, and the response rate to this combination was 33%. The response rate was similar between BRAF wild type (23%) and BRAF mutated patients (21%). In terms of clinical predictors of response, the study determined that male sex, BRAF mutations, absence of bone metastases, and normal lactate dehydrogenase levels were the most common predictors of success.

This trial demonstrated that in patients resistant to PD1 antibodies, the ipilimumab + PD1 combination has longer survival and higher response rates, with similar high-grade toxicity, than ipilimumab alone. The predictive factors identified in this study will be useful in selecting patients for the ipilimumab + PD1 combination after progression on PD1.



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LONG-TERM FOLLOW UP OF LIFILEUCEL (LN-144) CRYOPRESERVED AUTOLOGOUS TUMOR INFILTRATING LYMPHOCYTE THERAPY IN PATIENTS WITH ADVANCED MELANOMA PROGRESSED ON MULTIPLE PRIOR THERAPIES BY AMOD SARNAIK, MD (MOFFITT CANCER CENTER)

Sarnaik presented Abstract #10006 (NCT02360579), which suggested the efficacy of adoptive cell therapy using tumour-infiltrating lymphocytes in patients with advanced melanoma who have progressed on targeted therapies and checkpoint inhibitors. The study in question is the second cohort (66 patients) of C-144-01, a global phase 2 study of the safety and efficacy of lifileucel in patients with unresectable metastatic melanoma who have progressed on checkpoint inhibitors and BRAF/MEK inhibitors (if applicable). Lifileucel is an immunotherapy that utilizes the patient's tumour-infiltrating lymphocytes. The patient tumours were resected at local institutions, processed at central facilities for tumour-infiltrating lymphocyte production, manufactured, cryopreserved, and shipped back to local institutions in 22 days. Therapy included one week of lymphodepletion, one lifileucel infusion, and up to six doses of IL-2.

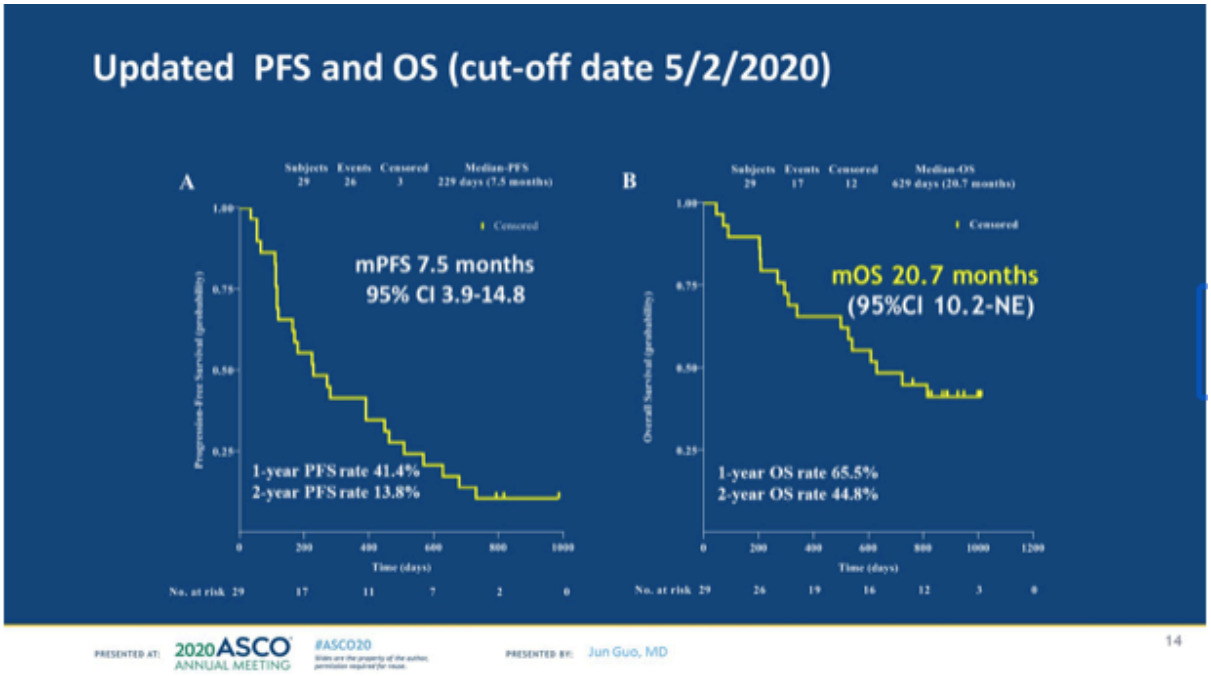
The results demonstrated an objective response rate of 36.4%, and a disease control rate of 80.3%, with a mean response time of 1.9 months. A follow up study of median 17 months demonstrated that the median duration of response had not been reached; six of the responders have progressed, two have died, and two have started other anti-cancer therapy.

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 BY XINAN SHENG, MD (SANGHAI JUNSHI BIOSCIENCES)

Sheng presented Abstract #10007 (NCT03086174), a clinical efficacy and safety trial for toripalimab, an immunoglobulin, combined with axitinib, a tyrosine kinase inhibitor, for the treatment of metastatic mucosal melanoma. The 33 patients enrolled in the study were given the combination of toripalimab + axitinib until voluntary withdrawal, disease progression, or unacceptable toxicity.

During the trial, 97% of patients experienced treatment-related adverse effects, 39.4% of these being grade 3-4, including proteinuria, diarrhea, and hypothyroidism. The objective response rate observed was 48.3%, while the disease control rate observed was 86.2%, with a median duration of response rate of 13.7 months. The median overall survival was 20.7 months and median progression-free survival was 7.5 months. Notably, gene expression profile scores of four angiogenesis-related and eight immune-related genes showed correlation with clinical response.

The results suggest that the combination of toripalimab + axitinib is a promising treatment option for patients with metastatic mucosal melanoma, and gene expression profile score of angiogenesis-related and immune-related may predict response to this combination.



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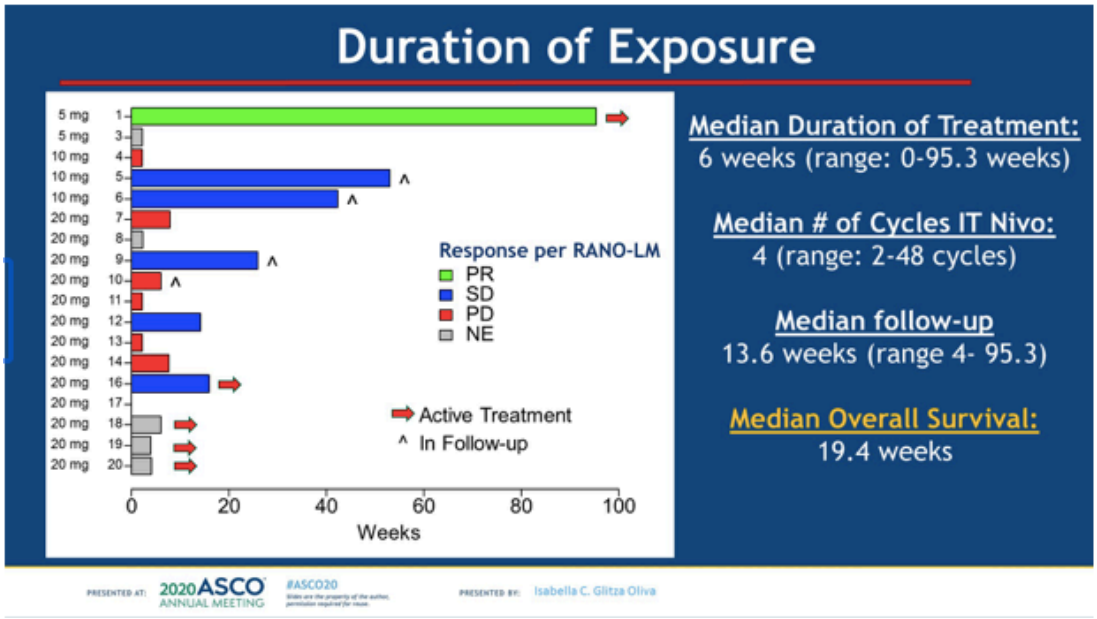
SINGLE-CENTER PHASE I/IB STUDY OF CONCURRENT INTRATHECAL (IT) AND INTRAVENOUS (IV) NIVOLUMAB (N) FOR METASTATIC MELANOMA (MM) PATIENTS (PTS) WITH LEPTOMENINGEAL DISEASE (LMD) BY ISABELLA CLAUDIA GLITZA, MD, MSC, PHD (THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER)

Glitza discussed Abstract #10008 (NCT03025256), a first-in-human study of intrathecal nivolumab in metastatic melanoma patients with leptomeningeal disease. The study aimed to determine the maximum tolerated dose and safety of this treatment. The 15 eligible patients that have been treated so far have metastatic melanoma and have shown evidence of leptomeningeal disease. 12 of these patients have received prior treatment for their metastatic melanoma, and 8 had positive cerebrospinal fluid cytology. The median follow-up of 18.7 weeks

demonstrated that the median overall survival is 46.1 weeks, and translational research endpoints and clinical response data are yet to be reported.

The results of this trial demonstrate the feasibility of prospective clinical trials for metastatic melanoma patients who also have leptomeningeal disease. This particular combination of intrathecal and intravenous nivolumab was well-tolerated and safe, and further results will include leptomeningeal disease composite response assessment.



(Slide from Glizta 2020)

CONCLUSION

Thank you for taking the time to read the Save Your Skin Foundation report on the American Society of Clinical Oncology 2020 virtual meeting. As always, we are so grateful to be able to attend ASCO, and excited by all of the promising care advances in the melanoma and patient advocacy spheres. If you would like more information about our report, please do not hesitate to contact taylorkathleen@saveyourskin.ca; if you would like more information about one of the studies mentioned above, they can be referenced by their clinical trial number at clinicaltrials.gov. Please bear in mind that Save Your Skin Foundation is an advocacy group, and are not able to give medical advice.