

[co]lab.notebook

name the cancer collaborative

project # ASCO18

date 25.06.2018

notes HIGHLIGHTS FROM ASCO 2018

new standards of care, practice changing trials and
important considerations for oncology

written by sabrina hanna

#ASCO18

#cancercolab

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CHICAGO- once again the american society for clinical oncology [ASCO] featured the latest news, information and data about advances in clinical cancer, however the program context also reflected a desire to broaden the reach of those advances and ensure the maximum number of patients derive maximum benefit. a substantial portion of the program was devoted to issues such as access to care; social, economic, and clinical disparities; use of technology to broaden the reach of cancer care and make it more efficient; greater emphasis on patient-reported outcomes and shared decision-making; and caring for the growing population of cancer survivors. led by ASCO president bruce johnson, a cancer survivor himself, the working theme for the 54th annual, meeting delivering discoveries: expanding the reach of precision medicine - the studies presented at ASCO have real and life-changing effects for people with cancer today and tomorrow. "the promise of precision medicine is only as good as our ability to make these treatments available to all patients," said dr. johnson during his presidential address.

recent advances in cancer research, and their subsequent translation into clinical practice, have had a transformative effect on the way cancer is treated- the following paper aims to provide insight on some of the practice changing studies presented during ASCO 2018.

Chicago

#ASCO18

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[tumour genomics. finding the target. hitting the target]

saturday june 2.2018

ado-trastuzumab emtansine [T-DM1] in patients with HER2 amplified tumours excluding breast and gastric | gastro-esophageal junction [GEJ] adenocarcinomas: results from the national cancer institute [NCI] molecular analysis for therapy choice [MATCH] trial. jhaveri, k, l. [see abstract 100]

NCI-MATCH is the largest national sign finding trial incorporating centralized genomic testing to direct patients to molecularly targeted phase II treatment arms. HER2 gene amplified is observed in many different tumour types.

conclusion. this arm did not meet its primary end point of ORR. T-DM1 was well tolerated. clinical activity was observed in HER2 amplified non-breast and gastric | GEJ adenoca patients warranting further study either alone or in combinations particularly in some histologies such as salivary gland tumours.

clinical trial information: **NCT02465060**

what's important.

- ▶ durable SD in ovarian, endometrial and colorectal cancers
- ▶ CR and PR reported in parotid gland tumours
- ▶ trend for tumour shrinkage with increased HER2 copy number was seen in the limited dataset
- ▶ correlation of HER2 copy number gain by MATCH assay with HER2 by IHC and FISH is ongoing
- ▶ further study of T-DMI in certain rare cancers

- NCI-MATCH is the largest precision medicine trial of its kind. Patients are assigned based on genetic changes found in the tumour through genomic sequencing

- such success reflects a promising future of genomics -

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a phase I study of LOXO-292, a potent and highly selective RET inhibitor, in patients with RET-altered cancers. LIBRETTO-001. drilon, a, e., et al [see abstract 102]

LOXO-292 is a global phase I study for patients with advanced solid tumours included RET fusion + NSCLC and papillary thyroid cancer [PTC], RET-mutant medullary thyroid cancer [MTC], and any other cancer with these alterations.

conclusion. LOXO-292 was well-tolerated and had marked anti-tumour activity in patients with RET-altered cancers, including those with resistance to prior multikinase inhibitors [MKIs] and brain metastases. rapid development with registrational intent is planned.

clinical trial information: **NCT03157128**

what's important.

- ▶ LOXO-292 demonstrates robust anti-tumour activity across RET altered cancers. 77% ORR in RET fusion positive cancers with intracranial activity. 45% ORR in RET mutant MTC. 71/78 [91%] of RET altered patients remain on therapy, including all responding patients
- ▶ activity independent of RET fusion partner, RET mutation or prior therapy
- ▶ safety and tolerability profile consistent with highly selective drug design
- ▶ [BLU-667] another second generation RET inhibitor was presented at AACR 2018

LOXO-292 is a potent and highly selective RET inhibitor showing impressive response rates

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impact of next-generation sequencing [NGS] on treatment selection in acute myeloid leukemia [AML]. assi, r, e., et al. [see abstract 103]

until recently, therapy options for AML patients were limited. the advent of NGS and novel targeted agents raise the question of how broader use of testing will impact treatment and outcomes.

conclusion. NGS can impact therapy decision in more than 30% of AML patients when performed in a timely manner. relapsed | refractory patients were more likely to receive targeted agents than newly diagnosed. possible reasons are delays in NGS results, urgency to start therapy and presumption that standard therapy may be better than investigational targeted agents. the result of current CT may change the way AML patients are treated.

what's important.

- ▶ patients treated with targeted therapy achieve higher overall response rates
- ▶ implementation of NGS in AML is feasible
- ▶ potential positive impact on relapse free survival [RFS] and some positive impact on newly diagnosed disease- response rate was not randomized and needs further confirmation
- ▶ median time to NGS results was 9 days
- ▶ 66% of AML patients have at least one actionable mutation [AMs] opening the doors for broader targeting
- ▶ NGS guided target therapy in more than 30% of patients, resulted in increased proportion of patients treated on target therapy [increased clinical trial accrual]

patients treated with
targeted therapies
achieved higher ORR

bullseye! hitting the target

christine m. lovly, MD, PhD

delivering discoveries. expanding the reach of precision medicine- this particular session really hits at the heart of that goal, thinking about expanding profiles of targets in precision cancer medicine.

paradigms for delivering discoveries. we have a target, we find the tumours where that target is found and then develop very selective therapies. pivoting and thinking otherwise, where we have a tumour, we need to find targets and then develop therapies against those targets or deploy therapies that we already have in hand.

how are targets of therapeutic interest defined? how do we actually define if a target is actionable or not? in some cases where we have multiple high-level evidence, like EGFR mutations or HER2 amplification in breast cancer, but that's not the case for every target identified and every variant that will be identified in NGS.

if we go back to this idea of expanding the reach of precision medicine through finding the target and hitting the target- we have the tumour, we have the target, we have the therapy we want. better outcomes for all patients. this is a complex system that involves multiple assets including HCPs, patients, data collection, analysis, curation and reporting. how can big data be deployed in a systematic way to expand the reach of precision medicine.

how can we as a community expand the reach of precision medicine?

- ▶ improve access to tumour molecular profiling to find known barriers
- ▶ provide decision support amongst our community to help facilitate treatment planning
- ▶ provide levels of evidence to support therapeutic decision-making for genomic variants and other biomarkers
- ▶ standardize how 'actionability' is defined
- ▶ sustain up-to-date annotation of the functional implications of genomic variants | other biomarkers
- ▶ systematically collect information on variants of uncertain significance [VUSs] to turn them from unknowns to knows
- ▶ continue to develop more and better drugs and innovative clinical trials
- ▶ engage patients | patient advocates on all levels to help achieve this goal

[EXPANDING
the reach of
precision medicine]

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[compelling combinations: raising the bar with immunotherapy]

sunday june 3.2018

setting the stage: where are we now with immunotherapy

solange peters, MD, PhD

there has been a revolution in cancer care since the introduction of immunotherapies. today, over 2000 immunotherapy agents are in development.

PD-1 | PD-L1 has brought about clinical significant benefit, however only in a minority of patients. this modest benefit [in comparison to previous treatments] has established new evidence based standards of care across many solid tumour types.

how can we improve immunotherapy response in patients?

biomarkers for patient selection

currently two biomarkers are being used for patient selection PD-1 | PD-L1 staining and tumour mutational burden [TMB]. the performance of PD-1 | PD-L1 as a biomarker is variable across tumour types, negative population can still benefit whereas TMB is a consistent biomarker with whole exome sequencing [WES]. immune cells and gene signatures are currently being studied, including TILs. many biomarkers will become available and there will be a need to prioritize them.

rational combinations

combinations present new treatment options for patients. a solid scientific rational and strong activity signals are required for new combinations to be tested. most combinations will have a PD-1 | PD-L1 backbone. however, many current combination trials are not based on biological mechanisms and are likely to fail.

moving immunotherapy to early line disease
moving immunotherapies from salvage therapy to earlier disease treatment has the potential to completely change the cancer landscape, prevent more patients from moving into metastatic disease setting therefor saving more patients. moving into the earlier disease setting can create new opportunities to define new standards in cancer care.

improving response to IO h

- biomarkers
- rational combinations
- early line tx

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putting it together: have combinations come of age
charles g. drake MD, PhD

improved efficacy of neoadjuvant compared to adjuvant immunotherapy to eradicate metastatic disease lui j. [2016]. this study in triple negative breast cancer [TNBC] used a variety of different immunotherapies and varying schedules to validate the efficacy of treatment in the neoadjuvant setting. the study demonstrated that immunotherapy was superior in the neoadjuvant setting vs. the adjuvant setting [in mice] to eradicate disease. the data demonstrated that a proportion of mice that received neoadjuvant therapy had significantly improved improved long term survival compared with the control group.

→ MUST READ

what's important:

- ▶ preclinical models and recent clinical trials have confirmed that combination approaches may be required for optimally effective and broadly applicable cancer immunotherapy
- ▶ tumour burden played no role in the improved efficacy of immunotherapy in the neoadjuvant setting [whereas TMB is important in determining response to treatment in metastatic disease setting- above]
- ▶ delays in neoadjuvant treatment still resulted in greater long-term survival
- ▶ CD8+ T cells can act as a biomarker to identify patients who will derive long-term benefit
- ▶ positive trial results will further revolutionize the field of cancer immunotherapy and improve outcomes for patients with cancer treating patients in the neoadjuvant setting can potentially eradicate disease and decrease the financial burden of cancer on healthcare systems

This trial has the potential to change the cancer landscape

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randomized phase II neoadjuvant study [geparnuevo] to investigate the addition of durvalumab to a taxane-anthracycline containing chemotherapy in triple negative breast cancer [TNBC] [loibl, s., et al. [see abstract 104]

combining immune checkpoint inhibitors with chemotherapy yielded high response rates in patients with metastatic TNBC. the addition of durvalumab, an anti PD-1 | L1 checkpoint inhibitor to standard neoadjuvant chemotherapy in patients with primary TNBC was evaluated.

conclusion. combination of chemotherapy with durvalumab/placebo yielded a high pathological response rate [pCR] in TNBC.

clinical trial information: **NCT02685059**

what's important.

- ▶ TNBC is associated with a high immunogenic potential
- ▶ response rates with PD-1 | L1 antibodies were higher when added to chemotherapy
- ▶ tumour infiltrating lymphocytes [TILs] correlate highly with other immune genes [eg. PD-1 | L1]
- ▶ TILs are predictive and prognostic in TNBC
- ▶ the addition of durvalumab was well tolerated and should be further investigated in patients with primary TNBC

phase III study of carboplatin-paclitaxel | nab-paclitaxel with or without pembrolizumab for patients with metastatic squamous non-small cell lung cancer [NSCLC] paz-ares, luis g., et al. keynote 407 [see abstract 105]

pembrolizumab plus pemetrexed and carboplatin resulted in superior objective response rate [ORR], progression-free survival [PFS] and overall survival [OS] for untreated patients with non-squamous NSCLC. pembro is active in squamous cell NSCLC, so combining with chemo is a rational next step.

conclusion. adding pembrolizumab almost doubled the ORR of chemo for patients with untreated metastatic squamous NSCLC. pembrolizumab | chemotherapy combination will become a new frontline standard of care irrespective of PD-L1 expression

what's important.

- ▶ pembrolizumab + chemo will become the new standard of care for the first line treatment of metastatic squamous NSCLC across all levels of PD-L1 expression
- ▶ median OS increased to 15.9 months when pembrolizumab was paired with chemotherapy [vs 11.3 months]. OS benefit observed pembrolizumab+chemo regimen persisted across all relevant patient subgroups including those with tumour PD-L1 expression categorized as low, intermediate and high
- ▶ progression free survival [PFS] and overall response rate [ORR] were also improved with pembrolizumab + chemotherapy and responses were more durable
- ▶ observed events were consistent with known safety profiles of pembrolizumab and chemotherapy with no new safety profiles identified

≡ NEW STANDARD of CARE ≡

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TOPACIO | keynote-162. a phase 1/2 study of niraparib + pembrolizumab in patients with advanced triple-negative breast cancer [TNBC] or recurrent ovarian cancer [ROC]. results from ROC cohort. konstantinopoulos, p.a., et al. [see abstract 106]

platinum-resistant ovarian cancer [OC] [PROC] currently has few treatment options. niraparib is an oral PARP inhibitor [PARPi] approved for maintenance treatment of recurrent ovarian cancer [ROC]. anti-PD-1 monotherapies have shown low level activity in ROC, and beyond BRCAmut, PARPi have shown minimal activity in PROC. preclinical data demonstrate synergy with PARPi + anti-PD-1 combinations.

* few tx options
in PROC
niraparib + pembro
promising combo

conclusion. with ORR of 25% in all PROC and ORR of 45% in tBRCAmut patients, niraparib + pembrolizumab appears promising. additional evaluation of this combination in ROC is warranted. no new safety signals were identified with the combination. clinical trial information: **NCT02657889**

what's important.

- niraparib + PD-1 inhibitor combination therapy provides clinical benefit in patients with platinum resistant and platinum refractory disease. 63% of whom received treatment of bevacizumab
- combination treatment resulted in an ORR of 25% and a median duration of response [DOR] of 9.3 months in the tested ovarian cancer population. [PARPi has an ORR 25-30% in BRCAmut platinum resistant patients but has demonstrated limited activity outside this setting. BRCAwt platinum resistant ORR ~ 5% and BRCAmut platinum refractory ORR 0-14%]
- platinum resistant | platinum refractory patients, efficacy was observed across biomarker selected populations, including tBRCAwt [ORR 24%] and HRDneg [ORR 27%]
- no new safety profiles were identified. hematological adverse events minimized with niraparib 200mg starting dose

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epacadostat + pembrolizumab versus pembrolizumab alone in patients with unresectable or metastatic melanoma: results of the phase III ECHO-301 | keynote-252 study. long, g. v., et al. [see abstract 108]

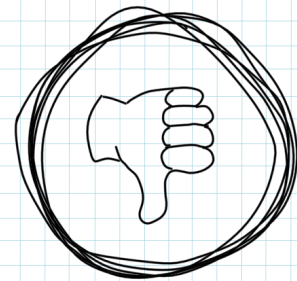
a phase 1/2 study, the combination of E, a selective oral inhibitor of the IDO1 enzyme, plus P, a PD-1 inhibitor, suggested promising anti-tumour activity with minimal additive toxicity in patients with untreated unresectable or metastatic melanoma.

conclusion. the addition of IDO to pembrolizumab did not result in greater clinical benefit over pembrolizumab alone in patients with unresectable or metastatic melanoma. recommendation to stop trial as study did not meet primary endpoint of PFS and OS was not expected to reach statistical significance. clinical trial information: **NCT02752074**

what's important.

this study did not meet its primary end point of PFS. the addition of IDO to pembrolizumab did not result in greater clinical benefit than pembrolizumab alone.

*after promising early clinical trial
IDO + pembro failed to meet its
primary endpoint
- trial discontinued -*



[plenary session]
sunday june 3. 2018

TAILORx: phase III trial of chemoendocrine therapy versus endocrine therapy alone in hormone receptor-positive, HER2-negative, node-negative breast cancer and an intermediate prognosis 21-gene recurrence score. sparano, j.a., et al. [see abstract LBA1]

a prospective, randomized trial of endocrine therapy [ET] versus chemoendocrine therapy [CET] in women with a mid-range oncotype DX recurrence score [RS] of 11-25. in hormone receptor [HR]-positive, HER2-negative, axillary node [AN]-negative breast cancer, the 21-gene expression assay [RS] is prognostic for distant recurrence, prognostic for low recurrence with endocrine therapy alone if low [0-10], and predictive of chemotherapy benefit if high [26 or higher].

conclusion. in women with HR-positive, HER2-negative, axillary node [AN]-negative breast cancer and a RS of 11-25, adjuvant ET was not inferior to CET in the intention to treat [ITT] analysis.

what's important.

women with hormone receptor [HR] positive, HER-2 negative and AN-negative breast cancer and midrange RS score do not need chemotherapy after surgery. chemotherapy could be avoided in about 70% of women when its use is guided by the RS test. findings could have an immediate impact on clinical practice, eliminating the necessity of receiving chemotherapy for some women and sparing them side effects of chemotherapy.

any woman with early stage breast cancer under 75 years should have the RS test. authors concluded that chemotherapy can be spared in all women older than 50 years of age with HR positive, HER-2 negative, AN negative breast cancer and a RS score of 0-25 [approximately 85% of women with BC in this age group]. all women 50 years of age or younger with HR positive, HER-2 negative, AN negative breast cancer and a recurrence score of 0-15 [about 40% of women with breast cancer in this age group].

this study is the first precision medicine trial and a prime example of the reach and impact of precision medicine.

*chemotherapy following surgery unnecessary
in 70% of women w^o HR⁺ HER2⁻ ANBC*

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pembrolizumab versus platinum-based chemotherapy as first-line therapy for advanced | metastatic NSCLC with a PD-L1 tumour proportion score [TPS] $\geq$ 1%: open-label, phase III keynote 402 study. lopes, g., et al [see abstract LBA4]

pembrolizumab was compared to chemotherapy at the lower TPS of $\geq$ 1%

conclusion. keynote-042 is the first study with a primary end-point of OS to demonstrate superiority of pembro over platinum-based chemo in patients with previously untreated advanced | metastatic NSCLC without sensitizing EGFR or ALK alterations and a PD-L1 TPS $\geq$ 1%. these data confirm and potentially extend the role of pembro monotherapy as a standard first-line treatment for PD-L1-expressing advanced/metastatic NSCLC. clinical trial information: **NCT02220894**

what's important.

- pembro significantly improved OS over platinum based chemotherapy as first line treatment for advanced | metastatic NSCLC with PD-L1 TPS $\geq$ 50%, 20%, 1%. patients lived a median 4-8 months longer compared with patients who received chemotherapy [PD-L1 $\geq$ 50% OS 20 months vs 12.2, PD-L1 $\geq$ 20% OS 17.7 months vs 13 months, PD-L1 $\geq$ 1% 16.7 months vs 12.1 months]
- greater magnitude of benefit for pembro at higher levels of PD-L1 expression consistent with previous studies of pembro monotherapy in metastatic NSCLC
- duration of response longer in patients treated with pembro than chemotherapy at all levels of PD-L1 expression
- despite longer exposure, frequency of treatment related AEs was lower with pembro [18% vs 41%]

[$\uparrow$ DoR at all levels of PD-L1 expression]

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[the arrival of biosimilars]
monday june 4.2018

biosimilars: regulatory definition products designed to mimic existing, approved biologic agents [not identical to reference biologic].
health canada defines biosimilars as a biologic drug demonstrated to be similar to a brand name drug already authorized for sale [known as the reference biologic drug].

the drug development process is heavily focused on manufacturing and pharmacology and looking at theoretical effects of the pharmacology and immunogenicity.

- ▶ biosimilars must be highly similar to the reference product notwithstanding minor differences in clinically inactive components.
- ▶ biosimilar development is heavily focused on manufacturing and pharmacology characterization and comparison with a goal of minimizing uncertainty.
- ▶ differences in the manufacturing process may lead to alterations in the protein structure, with theoretical effects on pharmacology and immunogenicity.

a comparative clinical trial of safety and efficacy is performed in a single disease and may grant approval across indications. this has the potential to rapidly increase the amount of biosimilars available.

so why do biosimilars exist?

main issues are cost and competition- are we really getting cost improvements and reductions in competition. who owns the biosimilars companies and what effects will this have on the market?

with more competition there are increased costs. if biosimilars don't decrease the price why bother with them. how much is this pushing the market to decrease costs?

how will they be used?

prescribers are acting tentatively to cautiously test the waters. with the advent of increasing clinical decision support [CDS], pathway programs will look at safety, efficacy and cost. franceschetti et al. reported biosimilar rituximab increased use in later line therapy, in patients with a better performance status [PS] and fewer comorbidities, and in indolent non hodgkin lymphoma [iNHL] incurable vs curable less aggressive lymphomas.

*what role will biosimilars
play in the oncology
landscape in canada?*

continue to pg. ☐

do the patients really have a voice in what drugs they are taking if prescribers are relying on CDS and pathways?

it may not be an option, and it may not need be.

totality of evidence. looking at the data and extrapolating it to indications using all the evidence available, but not necessarily randomized clinical data in each potential indication.

this will be important because it will be more rapid, save costs in developing these drugs and getting access.

biosimilars are additional high-quality treatment options. totality of evidence supports biosimilarity of trastuzumab-dkst to trastuzumab and extrapolation to all indications for which trastuzumab is approved. trastuzumab-dkst provides an additional high-quality treatment option for patients with HER2+ cancers.

prescriber and patient education is necessary in order to understand the complexities of how these are being developed and how they are being implemented.

there are possible increased patient costs which could abrogate the financial benefit of biosimilars. if efficacy is the same and safety is the same and cost is lower then value goes up.

biosimilars are here but uptake is variable. issues remain including clinical decision support [CDS] and pathway adoption, naming differences globally, competition and lower prices, and adoption to decrease cost, increase value to patients.

from nasdaq march 2018 pharmaceutical outlook

biosimilars should cut healthcare costs and provide a large number of patients with access to much-needed biologic treatments.

about \$250 billion could be saved in the next decade [2014-2024] if biosimilars for 11 products including neupogen, avastin, epogen, humira, neulasta, remicade and rituxan are approved. neupogen and remicade biosimilars alone represent potential savings of more than \$22 billion.

apart from amgen, novartis and pfizer, companies like biogen, merck and allergan are targeting the highly lucrative biosimilars market.

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[advances in fertility preservation for young women with cancer]
monday june 4.2018

integrating fertility into care for newly diagnosed young female cancer patient
karen l. smith, MD

chemotherapy and infertility risk in young women with cancer

most women receive therapy which may compromise fertility [breast cancer and other cancer types]. chemotherapy accelerates the decrease in primordial follicle reserve causing premature ovarian failure. impact on ovarian reserve varies with age [*increased risk of infertility with chemotherapy later in reproductive years. menstrual recovery after chemotherapy is age dependant*], drug class [*increased risk of infertility with use of alkylating agents*] and dose | duration [*increased risk of infertility with higher dose | longer duration*].

most women experience amenorrhea with chemotherapy [temporary or permanent]. recovery of menstrual cycles is more likely when younger. even if menstrual cycles recover, subsequent menopause occurs at a younger age [due to loss of ovarian use].

measuring ovarian reserve can be difficult and no optimal marker is available, even if menses may return, infertility can still occur, especially in women over 40.

anti-mullerian hormone [AMH] is emerging as a potential biomarker that may be useful for assessment of ovarian reserve in this population. a majority of patients will have a rapid decline and have undetectable levels of AMH by the end of their chemotherapy. during the following 18 to 24 months, a proportion of patients will recover some AMH levels. in general, those women who are younger at the time of chemotherapy and who have a higher baseline

AMH are more likely to recover and therefore less likely to have infertility.

other systemic therapies may also impact fertility

- endocrine therapy can cause temporary amenorrhea. infertility risk is largely due to delayed conception during endocrine therapy and natural ovarian aging can occur, contributing to infertility.
- targeted therapies and their impact on ovarian function and subsequent fertility has not been well defined. some literature with regard to HER2 therapy suggests that the addition of trastuzumab to chemotherapy does not increase the risk of infertility above the associated chemotherapy regimen risk.

SEER data estimated that 20,038 young women [<45 years stage I-III] are diagnosed with breast cancer in the US each year. of these 97% receive therapy that may impact fertility. using data from the national survey of family growth they estimated that 49% of these women may desire future fertility. therefore 9524 women with breast cancer [US] are at risk for treatment related infertility. all these women need education about the risk of treatment related infertility and if interested in fertility preservation, counselling regardless of options and possible referral to fertility specialists.

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a web based survey published in 2004 reported that 57% of women were worried about the impact of their treatment on fertility. 72% said that they had talked about it with a provider but only half felt that their concerns were being addressed. a prospective study published in 2014 revealed the same findings. data also suggest that concerns about fertility impacts psychosocial and quality of life outcomes. studies have indicated that women who have cancer and are going through treatment and who have reproductive concerns report lower quality of life, more symptoms of depression and higher levels of distress. also of concern, women with fertility concerns make treatment decisions based on these concerns [1/4 of breast cancer patients], emphasizing the need to address fertility concerns as a component of also optimizing breast cancer therapy.

ASCO guidelines

- ▶ be prepared to discuss fertility issues
- ▶ counsel patients as early as possible
- ▶ document discussions in the medical record
- ▶ refer interested or ambivalent patients for fertility specialists
- ▶ refer distressed patients for psychosocial support

oncology provider workflow. assess risk of treatment related infertility; counsel at risk patients about treatment related infertility; assess patients interest in fertility preservation; counsel interested [or ambivalent] patients about fertility preservation options; refer interested [or ambivalent] patients to fertility specialists.

value of addressing fertility early. the goal is to initiate fertility preservation prior to initiating systemic therapy. early referral will decrease delays in care. referring to a fertility specialist early decreases the time between diagnosis and initiation of fertility preservation as is the time between diagnosis and initiation of systemic therapy.

data suggests that fertility preservation has no impact on cancer outcomes. approximately 5% of women of reproductive age with cancer [lymphoma, breast cancer] pursue fertility preservation. uptake is low.

strategies to improve uptake.

- ▶ patient | provider education and materials
- ▶ mandate documentation of fertility discussion in medical records
- ▶ standardize process to identify, counsel, and refer patients [formalize referral system, partnerships between oncologists and fertility specialists]
- ▶ dedicated staff for counselling patients and educating providers

what's important.

most young female cancer patients are at risk for treatment related infertility

oncology providers should counsel patients about risk of treatment related infertility;

oncology providers should be able to counsel patients about fertility preservation options;

oncology providers should refer interested [and ambivalent] patients to fertility specialists.

*are we talking about fertility preservation
with young cancer patients in Canada ??*

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[next generation diagnostics beyond tissue]
tuesday june 5.2018

novel platforms for non invasive molecular testing
patrick c. ma, MD

molecular genomic tumour profiling platforms

tissue based biopsy. tissue may not be the issue - guidepost is moving with more clinical applications and validations particularly liquid biopsies and other non-invasive

tissue biopsies issues

- › invasive
- › primary site vs metastatic site
- › tissue adequacy [histological and biomarker information]
- › cost - reimbursement, implications [patients, payors, providers, society]

NCCN guidelines [2018] - metastatic disease PD-L1 testing & molecular testing

recommendation is for first line testing EGFR mutation, ALK, ROS1, BRAF testing should be conducted as part of broad molecular profiling. panel strongly advises 'broader molecular profiling' with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials.

broader molecular profiling is actually the emerging new standard of care and is a key component in improvement of care of patients.

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FDA approval of companion molecular diagnostic testing

november 15. 2017 NGS test to analyse genetic changes in patients' tumour. MSK-IMPACT [MSKCC] [profiled tumour samples for 468 different cancer-associated mutations or alterations].

december 1. 2017 FoundationOne Cdx [F1CDx] genomic test to identify cancer associated alterations in 324 genes and two types of genomic alterations | signatures in any type solid tumour. can be used as a companion diagnostic for 15 different targeted therapies used to treat 5 types of cancer. [tumour agnostic]

a major advantage of multi-gene test- it's intuitively simple. ability to derive a large amount of molecular and genomic information out of just a small amount of single tissue samples. it is often difficult to obtain adequate tissues from a tumour biopsy for multiple separate tests, the underlying concept for non-invasive testing.

multigene molecular diagnostic testing

MSK-IMPACT

FoundationOne CDx [F1CDx]

caris life sciences - caris molecular intelligence [MI] profile [multi-platform testing]

personal genome diagnostics [PSDx]

exome: cancerXOME-R, RNAcomplete-R, immunoselect-R

targeted: cancerselect-R 125

nanthealth: nantomics -GPS cancer test. comprehensive test integrating whole genome [DNA] sequencing [WGS], whole transcriptome [RNA] sequencing [RNA-seq] and quantitative proteomics.

continue to pg. ☐

emerging platforms. non invasive molecular diagnostic platforms

(i) breath biopsy

volatile organic compounds [VOC] profiling. catching a lot of attention in lung cancer. VOC can be considered as a metabolite biomarker profiled using appropriate platforms [gas chromatography, mass spectrometry [GCMS] and other chemical sensors]. exhaled human breath can contain thousands of VOC that can be exploited as biomarkers. VOCs can now be identified and measured in various headspace gas phases of tissues, blood and urine and even in exhaled breath. emerging body of literature has suggested the feasibility and promise of VOC profiling or fingerprinting as an attractive non invasive cancer diagnostic in the future.^{1 2 3 4}

national lung screening trial [NLST] conducted to determine whether screening with low dose CT [LDCT] could reduce mortality from lung cancer.

20% reduction in lung cancer specific mortality with LDCT

6.7% reduction in overall mortality with LDCT

(ii) saliva biopsy

pilot study showing that there are genetic variations that can be identified from saliva DNA. new technologies emerging allowing the assay for EGFR mutations from the saliva. DNA tumour suppressor methylation gene panel could have the potential to detect early stage tumours.

(iii) liquid biopsy

blood based molecular testing. CTC and ctDNA species inside the blood, with good quality CTC a whole host of molecular interrogations [in vitro and in vivo cell cultural PDX]. two components to liquid biopsies, soluble, allow for proteomics, metabolomics and exosome profiling and a cellular component for a new repertoire of profiling immunogenomics and immunoproteomix. tumour heterogeneity's relationship with tumour evolution is a key concept in non invasive molecular diagnostics, intratumoral heterogeneity, intertumoral heterogeneity and heterogeneity in the interactions with the tumour microenvironment.⁵

BREATH
SALIVA
LIQUID
BLOOD
biopsies
OH MY!

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new generation CTC platforms

cellsearch. abs based positive electromagnetic selection
parsortix. ANG-002 breast cancer clinical study
CTC-iChip. microfluidics, negative EM selection
VTX-1. microfluidics
cytotrapnano [canada]
capiocyte
DEPArray platform. silicon biosystems

CancerSEEK. can detect 8 common types of cancer [esophagus, breast, lung, stomach, liver, pancreas, colorectal and ovarian] through assessment of the levels of circulating proteins and mutations in cfDNA. positive results 70% across eight cancer types in more than 1000 patients. specificity was 99% and only 7 of 812 healthy controls had a positive score.

stool biopsy. can detect KRAS mutations. cologuard, US-FDA approved screening assay for colorectal cancer [2014].

urine biopsy. a lot of information molecularly, particularly for lung cancer- assay EGFR, BRAF and KRAS mutations with fairly high sensitivity and very good correlation and concordance with plasma assays. most recent data on the clinical relevance and validity of urine ctDNA molecular testing suggests that it could potentially be included in the molecular diagnostic model to combine urine and plasma based genotyping assays to precede tumour tissue biopsies.

what's important.

- novel non tissue based next generation invasive molecular diagnostics platforms have been emerging and expanding in clinical applications to match the revolution in cancer precision medicine immunotherapies
- increasingly applied to better monitor and interrogate tumour progression and evolution under therapy
- novel platforms include liquid, saliva, stool, urine and breath
- immunotherapies poses an unprecedented promise of cancer therapeutics but also poses a challenge in the need for novel and more validated diagnostics and biomarkers to optimize the benefit
- large scale prospective validation studies to ascertain the role in bedside applications

continue to pg. ☐

liquid biopsy to detect actionable genomic alterations

sai hong ignatius ou, MD PhD

no better way to expand the reach of precision medicine than through liquid biopsy.

liquid biopsy can detect mutations [EGFR, BRAF, HER2, KRAS, NRAS, PI3KCA⁶, ALK, ROS1, RET, NTRK, EGFR exon20, HER2 exon 20, MET exon14], resistance [EGFR T790M, ALK G1202R, ROS1, G2032R, ESR1 mut, ARv7], tumour mutational burden [TMB] minimal residual disease [MRD] and provide prognosis.

government approved FDA liquid biopsy test cobas EGFR mutation test, approved for three mutations [del19, L858R and T790M in lung cancer].

approved EU liquid biopsies cobas EGFR mutation test v2 [del19, L858R, T790M NSCLC] theascreen EGFR plasma RQO PER kit [del19, L858R NSCLC] oncobeam RAS CRC kit [NRAS, KRAS colorectal] idylla ctKRAS mutation test and idylla ctNRAS BRAF mutation test [NRAS, KRAS, BRAF colorectal cancer]

approved in china amoyDX super ARMS EGFR mutation detection kit [del19, L858R, T790M NSCLC]

liquid biopsy to determine TMB [POPLAR, OAK] to determine both PFS and OS, including more patients into the clinical trial who would be able to benefit. none commercially available in the US currently but a move towards this.

colorectal cancer tie et al. use ctDNA to detect residual disease and recurrence. study showed that if a patient presents with detectable ctDNA there is a high incidence of relapse regardless of adjuvant treatment and also whether clinical risk is high or low.⁷

what's important.

- despite widespread use of liquid biopsy, few tests are approved by government agencies. NGS will be liquid biopsies
- NGS based liquid biopsy is being used frequently in the US and china
- NGS based liquid biopsy most commonly used to detect actionable resistance mechanisms
- future use of NGS based liquid biopsy include detection of TMB, MRD and provide prognostication

continue to pg. ☐

[abstracts]

abstract 100.

ado-trastuzumab emtansine [T-DM1] in patients with HER2 amplified tumours excluding breast and gastric | gastro-esophageal junction [GEJ] adenocarcinomas: results from the national cancer institute [NCI] molecular analysis for therapy choice [MATCH] trial. jhaveri, k, l.

NCI-MATCH is the largest national signal-finding trial incorporating centralized genomic testing to direct patients to molecularly targeted phase II treatment arms. HER2 gene amplified is observed in many different tumour types.

results. seven [7] eligible patients were treated between 11.15-03.17. 33% had received > 3 lines of prior therapy. various histologies were treated: colon carcinoma [7], ovarian [6], rare tumours such as cholangiocarcinoma [1], carcinosarcoma of the uterus [1], salivary gland [3]. 8.1% [3] had a confirmed partial response including one patient each with salivary duct cancer of parotid gland, squamous cell cancer of parotid gland and extramammary paget's disease of the scrotum. additionally, 43% had stable disease [SD] including 3/3 evaluable ovarian and uterine cancer respectively. median duration of SD was 4.6 months. the 6-month PFS rate was 24.8%. median treatment duration was 4 cycles.

AEs. common toxicities included fatigue, anemia, fever and thrombocytopenia with no new safety signals.

conclusion. this arm did not meet its primary end point of ORR. T-DM1 was well tolerated. clinical activity was observed in HER2 amplified non breast and gastric | GEJ adenocarcinoma patients warranting further study either alone or in combinations particularly in some histologies such as salivary gland tumours.

clinical trial information: **NCT02465060**

continue to pg. ☐

abstract 102.

a phase I study of LOXO-292, a potent and highly selective RET inhibitor, in patients with RET-altered cancers. LIBRETTO-001. drilon, a, e., et al.

multikinase inhibitors [MKIs] have limited activity in RET fusion-positive and RET-mutant cancers, questioning the therapeutic potential of these targets. LOXO-292 selectively targets RET and has preclinical activity against activating RET fusions | mutations, potential resistance mutations, and brain metastases. LOXO-292 is a global phase I study for patients with advanced solid tumours included RET fusion+ NSCLC and papillary thyroid cancer [PTC], RET-mutant medullary thyroid cancer [MTC], and any other cancer with these alterations.

results. the primary endpoint was maximum tolerated dose [MTD] determination. secondary endpoints included safety, overall response rate [ORR, RECIST 1.1] and duration of response [DoR]. as of 05.01.18, 57 patients were treated at seven [7] doses, including 35 RET fusion+ tumours and 20 RET-mutant MTCs. 67% were MKI pre-treated. no dose limiting toxicity [DLTs] were observed. the MTD was not reached. the ORR in evaluable RET fusion+ patients was 69%, 65% in NSCLC and 83% in PTC. 84% [27/32] had radiographic tumour reduction. NSCLC responses occurred independent of upstream partner when known and included 3 patients with baseline brain metastases. tumour reduction was achieved in 79% of MTC patients, including 2 PRs, 1 in a patient with a hereditary RET V804M gatekeeper mutation treated with 3 prior MKIs. 79% of MTCs had a $\geq 50\%$ decrease in serum calcitonin [for ≥ 4 weeks]. most patients remained on treatment. the median DoR was not reached [all responses ongoing, longest > 6 months].

AEs. AEs [$\geq 10\%$ of patients] were fatigue [16%], diarrhea [16%] and dyspnea [12%]; most were grade 1-2. no AEs $\geq$ grade 3 were attributed to LOXO-292.

conclusion. LOXO-292 was well-tolerated and had marked anti-tumour activity in patients with RET-altered cancers, including those with resistance to prior MKIs and brain metastases. rapid development with registrational intent is planned.

clinical trial information: **NCT03157128**

see what's important.

continue to pg. ☐

abstract 103.

impact of next-generation sequencing [NGS] on treatment selection in acute myeloid leukemia [AML]. assi, r, e., et al.

until recently, therapy options for AML patients were limited. the advent of NGS and novel targeted agents raise the question of how broader use of testing will impact treatment and outcomes.

results. 1470 AML patients with available NGS based detection mutations were recruited from 10.2012 and 06.2016. 17 genes [ALK, CSF1R, FGFR1|2|3, FLT3, IDH1|2, JAK2, KDR, KRAS | NRAS, NPM1, PDGFRA, PTPN11, RET and TP53] were considered potentially actionable due to the possibility to be directly or indirectly targeted with standard or investigational agents.

of 1271 treated patients 982 [77%] had a median two [2] actionable mutations [AMs]. 41% started new therapy after NGS results availability. NGS guided targeted therapy in 53% of those enrolled on clinical trials [CT] and 6% received off label agents.

considering AMs only, relapsed | refractory patients were more likely to receive targeted therapy than newly diagnosed [51% vs 23%]. at different time points, the probability of receiving targeted agents for patients with AMs was 9%. patients who received targeted therapy had higher response rates to those who did not whether newly diagnosed [72% vs 60%].

conclusion. NGS can impact therapy decision in more than 30% of AML patients when performed in a timely manner. relapsed | refractory patients were more likely to receive targeted agents than newly diagnosed. possible reasons are delays in NGS results, urgency to start therapy and presumption that standard therapy may be better than investigational targeted agents. the result of current CT may change the way AML patients are treated.

- how will testing impact treatment and outcomes
- clearly there is still a role for targeted therapies in oncology

continue to pg. ☐

abstract 104.

randomized phase II neoadjuvant study [geparnuevo] to investigate the addition of durvalumab to a taxane-anthracycline containing chemotherapy in triple negative breast cancer [TNBC] loibl s., et al.

combining immune-checkpoint inhibitors with chemotherapy yielded high response rates in patients with metastatic triple negative breast cancer [TNBC]. the addition of durvalumab, an anti-PD-L1 checkpoint inhibitor, to standard neoadjuvant chemotherapy in patients with primary TNBC was evaluated in the geparnuevo study.

results. a total of 174 patients were enrolled between 06.2016 and 09.2017 and all patients had completed treatment. overall, 84 of 174 patients [48.3%] had a pathological complete response [pCR].

conclusion. chemotherapy in combination with checkpoint inhibitors increase pathological complete response rate.

AEs. a total of 86 secondary adverse events [SAEs] were reported [34.5%] and 65 immune related AEs of special interest [irAESI] were reported [27.6%].

continue to pg. ☐

abstract 105.

phase III study of carboplatin-paclitaxel/nab-paclitaxel with or without pembrolizumab for patients with metastatic squamous non-small cell lung cancer [NSCLC] paz-ares, luis g., et al.

combining pembrolizumab with conventional chemotherapy in the first-line setting significantly prolongs median overall survival [OS] in patients with metastatic squamous non-small cell lung cancer [NSCLC], according to data from the global phase III KEYNOTE-407 trial. the median OS reached 11.3 months with carboplatin and paclitaxel | nab-paclitaxel but increased to 15.9 months when pembrolizumab was paired with the chemotherapy. the OS benefit observed with the pembrolizumab | chemotherapy regimen persisted across all relevant patient subgroups, including those with tumour PD-L1 expression categorized as low, intermediate, and high.

results. consistent with OS, the pembrolizumab | chemotherapy combination significantly improved median PFS over chemotherapy alone [6.4 vs. 4.8 months] across all PD-L1 expression subgroups. patients also demonstrated a significantly higher objective response rate than those who received chemotherapy alone [58.4% vs. 35.0% at the first interim analysis] as well as a more durable response to treatment [median, 7.7 vs. 4.8 months].

AEs. frequency of adverse events was mostly similar between the pembrolizumab | chemotherapy and chemotherapy alone arms. the observed events matched the known safety profiles of both pembrolizumab and chemotherapy. the most common adverse events in both arms included anemia, alopecia, neutropenia, nausea, and thrombocytopenia, with the cytopenias comprising the majority of grade 3-5 adverse events in each arm.

immune-mediated adverse events and infusion reactions did occur more frequently with the addition of pembrolizumab to chemotherapy, with the most common immune-mediated adverse events [incidence $\geq 5\%$] associated with the pembrolizumab regimen included hypothyroidism [7.9%], hyperthyroidism [7.2%], and pneumonitis [6.5%].

conclusion. his data suggests that pembro plus carboplatin and paclitaxel or nab-paclitaxel should become a new standard of care for the first-line treatment of metastatic squamous NSCLC across all the different levels of PD-L1 expression.

further study. researchers will need to determine whether pairing chemotherapy and pembrolizumab confers additive activity or whether the combination promotes immunogenic cell death that leads to immune memory and a sustained long-term response.

⇒ NEW STANDARD of CARE ⇐

continue to pg. ☐

abstract 106.

TOPACIO | keynote-162. a phase 1/2 study of niraparib + pembrolizumab in patients with advanced triple-negative breast cancer [TNBC] or recurrent ovarian cancer [ROC]. results from ROC cohort. **konstantinopoulos, p. a., et al.**

platinum-resistant ovarian cancer [OC] [PROC] currently has few treatment options. niraparib is an oral PARP inhibitor [PARPi] approved for maintenance treatment of recurrent ovarian cancer [ROC]. anti-PD-1 monotherapies have shown low level activity in ROC, and beyond BRCAmut, PARPi have shown minimal activity in PROC. preclinical data demonstrate synergy with PARPi + anti-PD-1 combinations.

results. as of january 2018, 60 of 62 patients were evaluable for response assessment. median prior lines of chemotherapy was two [2] range 1-5. based upon platinum free interval [PFI] to last platinum treatment, 64% of patients had PROC [PFI < 6months] 19% had PRef disease [PFI <30 days] and 17% had platinum sensitive disease [PSens; PFI ≥ 6 months]. 20 patients remain on treatment and 11 have received treatment ≥6 months. among the 60 evaluable patients, ORR | DCR were 25% | 68%; among the 11 tumour BRCA [tBRCA]mut evaluable patients, ORR | DCR were 45% | 73%. responses were observed in 11 | 38 PROC patients., 2 | 11 PRef patients., and 1 | 10 PSens patients. [platinum status unknown in 1 responder].

conclusion. with ORR of 25% in all PROC and ORR of 45% in tBRCAmut patients, niraparib + pembrolizumab appears promising. additional evaluation of this combination in ROC is warranted. no new safety signals were identified with the combination. follow up is ongoing.

clinical trial information: **NCT02657889**

AEs. the most common grade ≥3 TEAEs were anemia [19%] and thrombocytopenia [9%].

continue to pg. ☐

abstract 108.

epacadostat + pembrolizumab versus pembrolizumab alone in patients with unresectable or metastatic melanoma: results of the phase III ECHO-301/keynote-252 study. Long, G. V., et al.

a phase 1/2 study, the combination of epacadostat [IDO], a selective oral inhibitor of the IDO1 enzyme, plus pembrolizumab, a PD-1 inhibitor, suggested promising anti tumour activity with minimal additive toxicity in patients with untreated unresectable or metastatic melanoma.

results. a total of 706 patients were randomized [354 to IDO + pembrolizumab and 352 to placebo + pembro]. 72.5% of tumours were PD-L1 positive, 44.5% BRAFmut [12.2% received prior BRAF | MEK therapy]. IDO + pembrolizumab did not result in a significantly longer PFS vs placebo + pembrolizumab. PFS in both groups was 37%. findings were consistent across PD-L1 and BRAF subgroups. OS was not expected to reach statistical significance based on results from the interim analysis. OS rate of 12 months was 74% in both groups. ORR 34.2% and 31.5%.

AEs. grade ≥ 3 treatment-related AEs occurred in 21.8% of patients receiving IDO + pembrolizumab and 17.0% receiving placebo + pembrolizumab.

additional analyses are underway to better understand these finding.

conclusion. the addition of IDO to pembrolizumab did not result in greater clinical benefit over pembrolizumab alone in patients with unresectable or metastatic melanoma.

clinical trial information: **NCT02752074**

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abstract 1000.

ribociclib [RIB] + fulvestrant [FUL] in postmenopausal women with hormone receptor-positive [HR+], HER2-negative [HER2-] advanced breast cancer [ABC]: results from MONALEESA-3. slamon, d.j., et al.

results from MONALEESA-3, a phase III randomized, double-blind, placebo-controlled study of RIB + FUL in postmenopausal women with HR+, HER2- ABC who received no or up to one line of prior endocrine therapy [ET] for ABC. the largest industry-sponsored phase III researching a CDK4/6 inhibitor in HR+ | HER2- advanced breast cancer.

results. 726 patients were enrolled. the primary objective was met: PFS was significantly improved in the RIB arm vs the PBO arm. consistent PFS benefit was observed in patients with no and up to one line of prior ET for ABC. in patients with measurable disease at baseline, ORR was 41% vs 29% [RIB vs PBO arm]. clinical benefit rate [CBR] was 69% vs 60%.

AEs. common all-grade adverse events were neutropenia [70% vs 2%], nausea [45% vs 28%], and fatigue [31% vs 33%]. in the RIB vs PBO arms, G3/4 neutropenia occurred in 47% | 7% vs 0% | 0% of patients, G3/4 increased alanine aminotransferase [ALT] in 7% | 2% vs < 1% | 0%, and G3/4 increased aspartate aminotransferase [AST] in 5% | 1% vs 1% | 0%.

conclusion. RIB + FUL vs PBO + FUL significantly prolonged PFS and demonstrated a manageable safety profile in postmenopausal patients with HR+, HER2- ABC who received no or up to one line of prior ET for advanced disease. RIB + FUL may, therefore, be a treatment option for this patient population.

clinical trial information: **NCT02422615**

what's important.

- patients receiving RIB + FUL had a statistically significant and clinically meaningful improvement in PFS vs placebo + FUL
- RIB treatment benefit was consistent across patient subgroups
- prolonged PFS was observed with first line RIB + FUL. benefit was also observed in patients who received treatment in second line
- RIB + FUL may be a new first or second line treatment option for postmenopausal women with HR+, HER2-ABC
- this is the first study to show that CDK 4 | 6 inhibitor + fulvestrant combinations are efficacious in patients de novo ABC and patients with disease that relapsed > 12 months after completion of prior [neo]adjuvant ET

continue to pg. ☐

abstract 4118.

prospective trial of preoperative FOLFIRINOX in patients with resectable pancreatic ductal adenocarcinoma [PDAC]: report of early endpoints. shahda, s. et al.

neoadjuvant therapy [NAT] may allow better selection for resection and provides early treatment of micro metastases. this study aimed to assess pathologic response, percent of patients who undergo resection, toxicity, perioperative mortality and survival after NAT in patients with resectable PDAC.

results. between 06.2014 - 10.2017, 51 patients consented and 48 enrolled [30 male | 18 female; median age 65 years [36-76], race: 43 W, 3 AA, and 2 other]. at data cutoff [12.31.17] 3 patients have not yet had surgical evaluation. of 45 patients, 36 have completed all planned preoperative chemotherapy. 35 patients have undergone resection.

conclusion. NAT is feasible in patients with resectable PDAC and may select out patients with aggressive biology who would not benefit from resection. pathologic responses were observed without pCR. survival data are maturing.

what's important.

- FOLFIRINOX regimen should be considered the new standard of care after pancreatic cancer resection in patients with good performance status

clinical trial information: **NCT02178709**

≡ NEW STANDARD of CARE ≡

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abstract 9002.

overall survival [OS] analysis of IMpower150, a randomized phase III study of atezolizumab + chemotherapy ± bevacizumab vs chemotherapy + bevacizumab in 1L non squamous [NSQ] NSCLC. socinski, m, a., et al.

atezolizumab inhibits PD-L1 to restore anticancer immunity; bevacizumab may enhance atezolizumab efficacy by inhibiting VEGF immunosuppression and promoting T-cell tumour infiltration. IMpower150 is the first randomized phase III trial evaluating atezo + chemo [carboplatin [C] + paclitaxel [P] ± bev vs CP + bev in 1L NSQ NSCLC. PFS benefit was observed with atezo + CP + bev vs CP + bev regardless of PD-L1 expression. co-primary endpoints were INV-assessed PFS in the ITT-WT [EGFR | ALK WT] and in WT patients with expression of a tumour T-effector gene signature [Teff-high WT] and OS in the ITT-WT. data cutoff: 01.22.2018.

results. 349, 359, and 337 ITT-WT patients were enrolled in arms A, B, and C, respectively. 13.5 months minimum follow-up, OS was improved in arm B vs C in the ITT-WT.

AEs. in all treated patients, grade 3-4 treatment-related AEs occurred in 43%, 57%, and 49% of patients in arms A, B, and C, respectively.

conclusion. IMpower150 showed a significant OS benefit with atezo + CP + bev vs CP + bev in 1L NSQ NSCLC. IMpower150 met its co-primary PFS and OS endpoints and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy in NSQ NSCLC, across all PD-L1 subgroups. no new safety signals were seen.

what's important.

- ▶ these data demonstrate that atezolizumab + bevacizumab + chemotherapy provide a new standard of care for key patients populations studied in this trial across all PD-L1 subgroups
- ▶ clinical benefit was observed in key subgroups of patients with EGFR | ALK genomic alterations and liver metastases at baseline, with the addition of bevacizumab to atezolizumab + chemotherapy
- ▶ the efficacy boundary has not yet been crossed for atezolizumab + chemotherapy vs bevacizumab + chemotherapy and will be tested again at the time of final analysis

clinical trial information: **NCT02366143**

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abstract 9502.

adjuvant therapy with nivolumab [NIVO] versus ipilimumab [IPI] after complete resection of stage III | IV melanoma: updated results from a phase III trial [checkmate 238]. weber, j, s., et al.

in the initial report of data from checkmate 238, at a minimum follow-up of 18 months, NIVO demonstrated significantly longer recurrence-free survival [RFS] vs IPI in patients with resected stage III or IV melanoma. updated efficacy results from this phase III study with an additional 6 months of follow-up were reported.

results. 906 patients were randomized 1:1 [stratified by disease stage and PD-L1 status at a 5% cutoff] for up to 1 year, or until disease recurrence or unacceptable toxicity. the primary endpoint was relapse free survival [RFS]; distant metastasis-free survival [DMFS] in patients with stage III disease was an exploratory endpoint. at a minimum follow-up of 24 mo, RFS continued to be significantly longer for NIVO vs IPI. the 24-month RFS rates were higher for NIVO vs IPI in subgroups defined by disease stage, PD-L1 expression, and BRAF mutation status. DMFS also continued to be significantly longer for NIVO vs IPI, with 24-month rates of 70.5% and 63.7%, respectively. subsequent therapies were received by 31.1% of patients in the NIVO group and 41.1% in the IPI group.

what's important.

- benefit for NIVO was observed across the majority of pre-specified subgroups including PD-L1 and BRAF mutation status
- these more mature data continue to demonstrate durable clinical benefit with NIVO and further support its use for resected stage III or IV melanoma

*durable clinical benefit
continues to be demonstrated
CAD*

AEs. no additional safety assessment

conclusion. with extended follow-up, NIVO demonstrated a sustained efficacy benefit vs IPI in patients with resected stage III | IV melanoma at high risk of recurrence, regardless of disease stage, PD-L1 expression, or BRAF mutation status.

clinical trial information: **NCT02388906**

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abstract 9503

4-year survival and outcomes after cessation of pembrolizumab [pembro] after 2-years in patients with ipilimumab [ipi]-naïve advanced melanoma in keynote-006. long, g, v., et al

keynote-006 established superiority of pembro over ipi in advanced melanoma. 4-y outcomes, and long-term data for patients who completed 2 years pembro, and data for second course.

results. 834 patients were randomly assigned. treatment was continued for 2 years [pembrolizumab only] completed defined as ≥ 94 weeks of pembro and discontinued with at least stable disease [SD] or until disease progression, intolerable toxicity, or patient | investigator decision to discontinue. end points were OS and ORR.

at data cutoff [04.12.2017], median follow-up was 45.9 months. 4-year OS rate was 42% in the pooled pembro arms [556] and 34% in the ipi arm [278]; ORR was 42% and 17%. median duration of response [DoR] was not reported [NR] for pembro or ipi; 62% pembro- and 59% ipi-treated patients had a response lasting ≥ 42 mo. in treatment-naïve patients, 4-year OS rates were 44% in the pooled pembro arms [368] and 36% in the ipi arm [181]; ORR was 47% and 17%. median DoR was NR for pembro or ipi; 65% pembro- and 68% ipi-treated patients had a response lasting ≥ 42 mo. of 556 patients, 103 [19%] completed the protocol-specified 2-year pembro [28 complete response [CR], 65 partial response [PR], 10 SD].

median follow-up was 20.3 months after pembro completion; 89 [86%] patients did not progress and 14 patients had PD [prior response 2 CR, 9 PR, 3 SD]. eight patients [prior response 3 CR [including 1 pt who discontinued early with CR and then progressed], 4 PR, and 1 SD] received second-course pembro but 3 discontinued [1 each due to progressive disease [PD], interstitial pneumonia, and infection]. median duration of second-course pembro was 9.7 mo; best overall response [BOR] was 1 CR, 1 PR, 5 SD, and 1 PD. 1 patient with SD had subsequent PD.

AEs. no grade 3/4 treatment related adverse events [TRAEs] or deaths. 5 patients had a TRAE during second-course pembro

conclusion. pembrolizumab provides durable anti-tumour activity in treatment-naïve or -experienced patients with advanced melanoma. of patients who completed 2 years pembro, 86% were progression free at 20 months. pembro is safe and provides additional anti-tumour activity as second-course treatment.

clinical trial information: **NCT01866319**

what's important.

- 86% of patients were progression free at 20 months after completion of pembrolizumab
- of the 556 patients who began the trial, 103 completed two years of the immunotherapy regimen
- retreatment with pembro upon disease progression can provide additional anti-tumour activity with acceptable safety
- pembro continues to provide durable anti-tumour activity in treatment naïve and treatment experience patients with advanced melanoma
- with more follow-up time, keynote-006 could help answer the question of whether two years was enough time to support long-term, durable response

continue to pg. ☐

abstract LBA1

TAILORx: phase III trial of chemoendocrine therapy versus endocrine therapy alone in hormone receptor-positive, HER2-negative, node-negative breast cancer and an intermediate prognosis 21-gene recurrence score. sparano, j.a., et al.

a prospective, randomized trial of endocrine therapy [ET] versus chemoendocrine therapy [CET] in women with a mid-range oncotype DX recurrence score [RS] of 11-25. in hormone receptor [HR]-positive, HER2-negative, axillary node [AN]-negative breast cancer, the 21-gene expression assay [RS] is prognostic for distant recurrence, prognostic for low recurrence with endocrine therapy alone if low [0-10], and predictive of chemotherapy benefit if high [26 or higher].

results. 10,253 eligible women enrolled between april.07.2006-october.06.2010. 6711 [65.5%] had an RS of 11-25. there were 836 invasive disease free survival [iDFS] events at final analysis with a median follow up of 90 months. ET was non-inferior to CET iDFS. ET was also non-inferior for distant recurrence free interval [DRFI], recurrence free interval [RFI] and overall survival. nine year rates were similar for iDFS [83.3% vs 84.3%], DRFI [94.5% vs 95%], RFI [92.2% vs 92.9%] and OS [93.9% vs 93.8%]. recurrence accounted for 338 [41.6%] the first iDFS event, of which 199 [23.8%] were distant recurrences. treatment interactions were significant for age but not menopause, tumour size, grade, or RS.

conclusion. in women with HR-positive, HER2-negative, AN-negative breast cancer and a RS of 11-25, adjuvant ET was not inferior to CET in the intention to treat [ITT] analysis.

RS 11-25 ET was non-inferior to chemotherapy + ET
RS 0-10 distant recurrence rates very low [2-3%] with ET alone at 9 years RS 25-100 significantly higher event rates, driven by more recurrences despite adjuvant chemo + ET.

age + RS + chemo treatment interaction observations some chemo benefit in women 50 or younger with RS 15-25 greatest impact on distant recurrence with RS 21-25.

* [practice changing]

continue to pg. ☐

abstract LBA3.

CARMENA: cytoreductive nephrectomy followed by sunitinib versus sunitinib alone in metastatic renal cell carcinoma [mRCC]—results of a phase III non inferiority trial. mejean, a., et al.

cytoreductive nephrectomy [CN] has been the standard of care in mRCC in the past twenty years, supported by randomized and large retrospective studies. however the efficacy of targeted therapies has challenged this standard. CARMENA was designed to answer the question of whether upfront CN should continue to be performed before sunitinib.

results. patients were randomized 1:1 to either CN followed by sunitinib [arm A] or sunitinib alone [arm B]. 450 patients were included from 09.09 to 09.17, 226 and 224 in arm A and B. in arm A, 6.7% did not have CN and 22.5% never received sunitinib. in arm B, 4.9 % never received sunitinib and 17% had secondary nephrectomy. at the time of the analysis, 326 deaths have been observed with a median follow-up of 50.9 mo. OS was not inferior in arm B, overall as well as by MSKCC risk groups. no difference in response rate and PFS was observed.

AEs. safety of sunitinib was as expected in both arms.

conclusion. sunitinib alone is not inferior to CN followed by sunitinib in synchronous mRCC both in intermediate and poor MSKCC risk groups. CN should no longer be the standard of care when medical treatment is required.

clinical trial information: **NCT00930033**

what's important.

- ▶ many patients with advanced kidney cancer do not need surgery
- ▶ median survival was 18.4 months without surgery vs. 13.9 months with surgery. subgroups with an intermediate [median survival was 23.4 months vs. 19 months] and poor prognosis [median survival was 13.3 months vs. 10.2 months] groups
- ▶ the difference in median survival seems to suggest a greater benefit with sunitinib alone. however, this cannot be concluded, as this trial was not designed to prove that one treatment is superior to the other
- ▶ the rate of tumour response to therapy [tumour shrinkage] was the same in the two treatment groups [27.4% and 29.1%] and the median time until the cancer worsened was slightly longer for patients who received sunitinib alone compared with those who also had surgery [8.3 months vs. 7.2 months]
- ▶ clinical benefit was experienced by 47.9% of patients treated with sunitinib only, compared with 36.6% of patients treated by surgery and sunitinib

the authors remarked that kidney surgery is still the gold standard for people who do not need systemic therapy, such as those with only one metastasis. [those patients were not included in this clinical trial].

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abstract LBA4.

pembrolizumab versus platinum-based chemotherapy as first-line therapy for advanced | metastatic NSCLC with a PD-L1 tumour proportion score [TPS] $\geq 1\%$: open-label, phase III keynote-042 study. lopes, g., et al.
pembrolizumab was compared to chemotherapy at the lower TPS of $\geq 1\%$

results. 1274 patients were randomized- 637 to each arm. 599 [47.0%] had TPS $\geq 50\%$, 818 [64.2%] had TPS $\geq 20\%$. after 12.8-months median follow-up, 13.7% were still on pembrolizumab and 4.9% were receiving pemetrexed [peme] maintenance. pembrolizumab significantly improved OS in patients with TPS $\geq 50\%$, TPS $\geq 20\%$, and TPS $\geq 1\%$.

AEs. grade 3-5 drug-related AEs were less frequent with pembrolizumab [17.8% vs 41.0%] the external data monitoring committee [DMC] recommended continuing the trial to evaluate PFS [secondary end-point].

conclusion. keynote-042 is the first study with a primary end-point of OS to demonstrate superiority of pembrolizumab over platinum-based chemo in patients with previously untreated advanced | metastatic NSCLC without sensitizing EGFR or ALK alterations and a PD-L1 TPS $\geq 1\%$. these data confirm and potentially extend the role of pembrolizumab monotherapy as a standard first-line treatment for PD-L1-expressing advanced/metastatic NSCLC.

clinical trial information: **NCT02220894**

see what's important.

[POTENTIAL STANDARD of CARE]

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abstract LBA1006.

phase III study of tasisib [GDC-0032] + fulvestrant [FUL] v FUL in patients with estrogen receptor [ER]-positive, PIK3CA-mutant [MUT], locally advanced or metastatic breast cancer [MBC]: primary analysis from SANDPIPER. baselga, j., et al.

SANDPIPER is a double-blind, placebo [PBO]- controlled, randomized, phase III study assessed tasisib + FUL in patients with ER-positive, HER2-negative, PIK3CA-MUT locally advanced or MBC. tasisib, a potent, selective PI3K inhibitor, has enhanced activity in PIK3CA-MUT BC cell lines and confirmed partial responses in PIK3CA-MUT BC as a single-agent or with FUL. the primary endpoint was investigator-assessed progression-free survival [INV-PFS] in patients with PIK3CA-MUT tumours. secondary endpoints included objective response rate [ORR], overall survival [OS], clinical benefit rate [CBR], duration of objective response [DoR], PFS by blinded independent central review [BICR-PFS], and safety.

results. 516 postmenopausal women with disease recurrence or progression during or after an aromatase inhibitor were randomized 2:1 to receive tasisib [340 women]. or PBO + FUL [176 women]. tasisib + FUL significantly improved INV-PFS as confirmed by BICR-PFS. OS is immature.

AEs. the most common grade ≥3 adverse events in the tasisib + FULV arm in safety-evaluable patients who received ≥ 1 dose of treatment were diarrhea [12], hyperglycemia [10%], colitis [3%], and stomatitis [2%]. AEs led to more tasisib discontinuations [17% v 2%] and dose reductions [37% v 2%], vs PBO.

conclusion. tasisib + FUL significantly improved INV-PFS, v PBO + FUL, in patients with ER-positive, HER2-negative, PIK3CA-MUT locally advanced or MBC. the safety profile is largely consistent with previous studies.

clinical trial information: **NCT02340221**

what's important.

- ▶ tasisib, combined with standard hormone therapy fulvestrant, halted the growth of advanced breast cancer growth by 2 months longer than hormone therapy alone, and decreased the chance of cancer worsening by 30%
- ▶ the response rate to treatment [tumour shrinkage] was more than doubled when tasisib was added [28% vs. 11.9%]
- ▶ tasisib extended the time until the cancer worsened by a median of two months [7.4 months with tasisib and fulvestrant vs. 5.4 months with fulvestrant + placebo]
- ▶ tasisib targets a common genetic abnormality in breast cancer [PIK3CA gene mutation] and is the first and most potent treatment in a relatively new class of PI3K inhibitors
- ▶ 40% of all patients with advanced breast cancer estrogen receptor positive have PIK3CA mutations, which means they could benefit from tasisib.
- ▶ targeting this pathway in breast cancer is effective, although benefit is modest and there is a risk of considerable side effects
- ▶ tasisib provided more benefit to study participants who received treatment in north america and europe, where cancer worsening was delayed by a median of 3.5 months [7.9 with tasisib + fulvestrant vs. 4.5 months with only fulvestrant]. in other countries including eastern europe and latin america, tasisib appeared to provide very little or no added benefit. more research is needed understand the reasons for this discrepancy

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abstract LBA1509.

pan-cancer micro-satellite instability to predict for presence of lynch syndrome

a genomic study of more than 15,000 tumour samples demonstrated that patients with tumours that have high micro-satellite instability [MSI-H] are more likely to have lynch syndrome. lynch syndrome is a hereditary condition that increases a person's risk of developing several different types of cancer. the hallmark of lynch syndrome-associated tumours is MSI-H. MSI is a genomic marker that points to a defect in a cell's ability to repair DNA.

researchers used MSK-IMPACT, a comprehensive genomic test, to analyze over 15,000 tumour samples collected from patients with more than 50 different types of advanced cancer. the test uses next-generation sequencing [NGS] to look for mutations in hundreds of cancer-related genes, as well as other molecular changes, including MSI.

additionally, researchers tested blood samples for inherited mutations in genes involved in DNA repair. tumours caused by lynch syndrome have mismatch repair deficiency [MMR-D] and are MSI-H. researchers also tested blood samples from study participants for inherited mutations in genes involved in DNA repair: MLH1, MSH2, MSH6, PMS2, and EPCAM. mutations in these genes cause lynch syndrome. tumours caused by lynch syndrome have mismatch repair deficiency [MMR-D] and are MSI-H.

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abstract LBA1509. [cont'd]

results. the majority of tumours [93.2%] were found to be MSS; 4.6% were MSI-I; and 2.2% were MSI-H. inherited mutations in lynch syndrome associated genes were found in 16% of people with MSI-H tumours, compared to 1.9% of those with MSI-I tumours and only 0.3% of those with MSS tumours. 25% of the 1,025 MSI-H/MSI-I tumours were colorectal or endometrial cancers, the most common cancers linked to lynch syndrome. MSI testing is routinely performed on such tumours. nearly 50% of patients with MSI-H/MSI-I tumours who were identified as having lynch syndrome had cancer types not previously, or rarely, linked to the syndrome, including: mesothelioma, sarcoma, adrenocortical cancer, melanoma, prostate, and ovarian germ cell cancer. of these patients, 45% did not meet lynch syndrome genetic testing criteria based on family or personal cancer history. 57 MSI-H/MSI-I tumour samples were also tested for abnormal DNA repair proteins - and MMR-D was found in nearly all [98.3%] of those tumours. these findings suggest that if either MSI-H or MMR-D is found in the tumour, hereditary genetic testing for lynch syndrome should be performed.

conclusion. MSI-H/MMR-D is predictive of LS across tumour types and suggests a more heterogeneous spectrum of LS-associated cancers than previously appreciated. nearly 40% of LS patients with MSI-H/MMR-D non-CRC/EC tumours did not meet clinical criteria for genetic testing, suggesting that MSI-H/MMR-D tumours, regardless of cancer type or family history, should prompt germline testing for the evaluation of LS.

whats important.

- ▶ the chance of developing certain cancers linked to lynch syndrome can be lowered through frequent screening. 16% of patients with MSI-H tumours have lynch syndrome, and 50% of patients with lynch syndrome had cancer types not previously, or rarely, linked to the syndrome
- ▶ diagnosing lynch syndrome provides the unique opportunity of helping not only cancer patients, but also at-risk family members, as cancer risk can be lowered through increased cancer surveillance and, in some cases, preventive surgery
- ▶ MSI-H/MMR-D tumours, regardless of cancer type or family history, should prompt germline testing for the evaluation of LS

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abstract LBA3503.

a UNICANCER phase III trial of hyperthermic intra-peritoneal chemotherapy [HIPEC] for colorectal peritoneal carcinomatosis [CPC]: PRODIGE 7. quenet, f., et al.

prodige 7 is a randomized phase III, multicentre trial. this is the first trial to evaluate the specific role of HIPEC, after cytoreductive surgery [CRS], for the treatment of peritoneal carcinomatosis [PC] of colorectal origin. patients were treated with CRS plus HIPEC with oxaliplatin or CRS alone, in association with systemic chemotherapy. primary endpoint was overall survival [OS] and relapse-free survival [RFS] and toxicity secondary endpoints.

results. 265 patients from 17 centres were included between february 2008 and january 2014: 132 in arm without HIPEC and 133 in arm with HIPEC. the overall post-operative mortality rate was 1.5% and was not different between the two arms. after a median follow up of 63.8 months the median OS was 41.2 months in the non-HIPEC arm and 41.7 months in the HIPEC arm. median RFS was 11.1 months in non-HIPEC arm and 13.1 months in HIPEC arm. and 1-year RFS rates were 46.1% in non-HIPEC arm and 59 % in the HIPEC arm.

AEs. morbidity rates did not differ statistically at 30 days. at 60 days, grade 3-5 morbidity was significantly higher with HIPEC [24.1% vs. 13.6%].

conclusion. the therapeutic curative management of PC from colorectal cancer by CRS shows satisfactory survival results. while the addition of HIPEC with oxaliplatin does not influence the OS.

clinical trial information: **NCT00769405**

what's important.

- this is the first randomized study assessing the role of HIPEC chemotherapy in advanced colorectal cancer, and it shows that it does not provide added benefit over surgery
- further study. a subgroup analysis performed in the PRODIGE 7 study shows the possibility that HIPEC may be effective for patients with a 'mid-range peritoneal cancer index', however, the numbers analyzed were too small to be conclusive. further studies can also look into whether other types of chemotherapy could be more beneficial than oxaliplatin, which was used in PRODIGE 7

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abstract LBA4002.

preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer [PREOPANC-1] : a randomized, controlled, multicentre phase III trial. bonsing, h.j., et al.

preliminary findings of a multicentre phase III randomized controlled trial to evaluate the effect of preoperative chemoradiotherapy was conducted. standard of care for patients with [borderline] resectable pancreatic adenocarcinoma is resection followed by adjuvant chemotherapy. previous studies suggest a benefit of neoadjuvant treatment.

results. 246 patients were included in the intention-to-treat analysis [ITT] [127 patients in arm A and 119 in arm B]. currently, 142 of the 176 needed events for the primary outcome are observed. OS was significantly better in arm B [median 13.5 vs. 17.1 months]

AEs. no significant difference was observed in grade ≥ 3 adverse events between both groups

conclusion. preliminary data show that preoperative chemoradiotherapy significantly improves outcome in [borderline] resectable pancreatic cancer compared to immediate surgery.

what's important.

- results of the study suggest a benefit of neoadjuvant radiochemotherapy over upfront surgery and has the potential to be a practice changing trial
- 2-year survival rate was higher for those who received this treatment plan. 42% of patients achieved this survival compared with 36% of those who had immediate surgery. where the tumour was removed successfully during surgery, the median survival was even greater; 42.1 months with preoperative chemoradiotherapy compared with 16.8 months without
- in the patients that immediately underwent surgery, the tumour was resected in 72% of cases, compared with 62% in those who received preoperative chemoradiotherapy. however, among those who had the tumour resected, complete microscopic removal was achieved in a greater proportion of the patients who had preoperative treatment; 63% compared to 31%
- further study. after the final analysis and publication of this trial, the next step is to attempt to find even more effective preoperative treatments

Potential/
practice
changing

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abstract LBA4008.

chemoprevention of esophageal cancer with esomeprazole and aspirin therapy: efficacy and safety in the phase III randomized factorial ASPECT trial. jankowski, j., et al.

findings from an updated analysis from a randomized phase III trial show that taking a high dose of the acid-reducing medicine esomeprazole [Nexium®] with low dose aspirin for at least seven years can moderately reduce the risk of developing high grade dysplasia [a pre-cancerous lesion] or esophageal cancer [EC], or delay death from any cause in people with barrett's esophagus [BE]. the efficacy of aspirin and high dose acid suppression in preventing EA in patients with BE was evaluated. patients were randomized unblinded 1:1:1:1 in a 2X2 factorial design to high dose [40mg twice daily] or low dose [20mg once daily] esomeprazole proton pump inhibitor acid suppression [PPI], alone or combined with low dose aspirin 300mg/day [330mg in Canada].

results. 2563 Barrett's patients followed-up for a median of 8.9 years. there were 313 events of the composite primary endpoint. high dose PPI was statistically significantly superior to low dose PPI. aspirin therapy showed a trend to benefit but was not statistically significant. the combination of aspirin with high dose PPI had the strongest effect compared to low dose PPI with no aspirin.

AEs. there were few serious adverse events reported [1.0% of patients], with 99.9% data collected. the most common side effect of proton pump inhibitors is diarrhea. the most serious side effects of aspirin include allergic reactions, bleeding in the stomach, and bleeding in the brain [particularly for people with high blood pressure]. in addition, people who are already taking another non-steroidal anti-inflammatory drug [NSAID], should not be taking aspirin.

what's important.

- esophageal adenocarcinoma [EA] is the sixth most common cause of global cancer death
- development of EA could be delayed by using these simple, over-the-counter medicines. esophageal cancer is very difficult to screen for and treat – less than 1 in 5 [19%] of patients survive five [5] years after diagnosis
- national bodies should consider the findings when developing guidelines for esophageal cancer prevention

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abstract LBA8501.

genome-wide sequencing for early stage lung cancer detection from plasma cell-free DNA [cfDNA]: the circulating cancer genome atlas [CCGA] study. oxnard, g.r., et al.

an initial report from the large, ongoing circulating cell-free genome atlas [CCGA] study provides preliminary evidence that a blood test may be able to detect early-stage lung cancer. this is one of the first studies to explore blood tests analyzing free-floating or cell-free DNA as a tool for early detection of cancer.

results. the CCGA study has enrolled more than 12,000 [of the planned 15,000 participants] [70% with cancer, 30% without cancer], across 141 sites in the united states and canada. three prototype sequencing assays were performed on blood samples from approximately 1,700 participants. twenty different cancer types across all stages were included in the sub-study [see abstracts 536, 12021, and 12003].

among the 127 participants with lung cancer, the biologic signal for lung cancer was comparable across the assays, and the signal increased with cancer stage. at 98% specificity, the WGBS assay detected 41% of early stage [stage I-IIIa] lung cancers and 89% of late-stage [stage IIIB-IV] cancers. the WGS assay was similarly effective, detecting 38% of early-stage cancers and 87% of late-stage cancers, whereas the targeted assay detected 51% of early-stage cancers and 89% of late-stage cancers. initial results showed that all three prototype assays could detect lung cancer with a low rate of false positive findings [a false positive occurs when the test suggests a person has cancer when there is no cancer].

conclusion. initial results from the CCGA study show it is possible to detect early-stage lung cancer from blood samples using genome sequencing.

clinical trial information: **NCT02889978**

what's important.

lung cancer is the most common cancer, globally. most lung cancers have already spread widely and are at an advanced stage before being diagnosed.. survival rates are significantly higher when lung cancer is diagnosed early [165 vs 4%]. having a blood test that can be done through a simple blood draw at the doctor's office may improve lung cancer screening rates, but before such a test could be widely used, additional validation in larger data sets and in studies with people who have not been diagnosed with cancer would be needed.

of the 580 control samples [from people without cancer at study enrolment], five [<1%] had a cancer-like signal across all three assays. of those five participants, two were subsequently diagnosed with cancer [one with stage III ovarian cancer, and one with stage II endometrial cancer] highlighting the potential for such a test to identify early stage cancers.

*a blood test may be able to detect
EARLY STAGE LUNG CANCER*

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[abbreviations]

AACR	american association of cancer research
ABC	advanced breast cancer
AE	adverse events
ALK WT	ALK wild type
AM	actionable mutation
AMH	anti mullerian hormone
AML	acute myeloid leukemia
AN	axillary node
atezo	atezolizumab
BC	breast cancer
BE	barrett's esophagus
BEV	bevacizumab
BICR-PFS	blinded independent central review progression free survival
BOR	best overall response
CBR	clinical benefit rate
CCGA	circulating cell free genome atlas
CDS	clinical decision support
CN	cytoreductive nephrectomy
CT	clinical trial
cfDNA	cell free DNA
ctDNA	circulating tumour DNA
CET	chemoendocrine therapy
CP	carboplatin + paclitaxel
CPC	colorectal peritoneal carcinomatosis
CR	complete response
CRS	cytoreductive surgery
DMC	data monitoring committee
DoR	duration of response
DMFS	distant metastasis free survival
DRFI	distant recurrence free interval
EA	esophageal adenocarcinoma
EC	esophageal cancer
ER	estrogen receptor
ET	endocrine therapy
FUL	fulvestrant
GEJ	gastro-esophageal junction adenocarcinoma
HIPEC	hyperthermic intra-peritoneal chemotherapy
HCPs	health care provider practitioner
HR	hormone receptor
iDFS	invasive disease free survival
iNHL	indolent non hodgkin lymphoma
irAEs	immune related adverse events

INV	investigator
INV-PFS	investigator-assessed progression free survival
IPI	ipilimumab
ITT	intention to treat
ITT-WT	intention to treat wild type
LS	lynch syndrome
MATCH	molecular analysis for therapy choice trial
MBC	metastatic breast cancer
MMR-D	mismatch repair deficiency
mRCC	metastatic renal cell carcinoma
MRD	minimal residual disease
MSI-I	microsatellite instable
MSI-H	high microsatellite instability
MSKCC	memorial sloan kettering cancer centre
MSS	microsatellite stable
NAT	neoadjuvant therapy
NCI	national cancer institute
NGS	next generation sequencing
NIVO	nivolumab
NR	not reported
NSAID	non steroidal anti inflammatory drug
NSCLC	non small cell lung cancer
NSQ	non squamous
OC	ovarian cancer
ORR	objective response rate
OS	overall survival
PARPi	poly ADP ribose polymerase inhibitor
PBO	placebo
PC	peritoneal carcinomatosis
pCR	pathological response rate
PD	progressive disease
PDAC	pancreatic ductal adenocarcinoma
pembro	pembrolizumab
peme	pemetrexed
PFI	platinum free interval
PFS	progression free survival
PPI	proton pump inhibitor
PR	partial response
PRef	platinum refractory disease
PROC	platinum resistant ovarian cancer
Psens	platinum sensitive disease
RIB	ribociclib

RET	rearranged during transfection
RFS	relapse free survival
ROC	recurrent ovarian cancer
RS	recurrence score
SD	stable disease
T-DMI	ado-trastuzumab emtansine
TEAEs	treatment emergent adverse events
TRAEs	treatment related adverse events
TILs	tumour infiltrating lymphocytes
TMB	tumour mutational burden
TNBC	triple negative breast cancer
TPS	tumour proportion score
VUS	variants of uncertain significance
VOC	volatile organic compounds
WES	whole exome sequencing
WGS	whole genome sequencing
WGBS	whole genome bisulfite sequencing
WT	wild type

[endnotes]

¹ detection of cancer through exhaled breath: a systemic review. krilaviciute, a., et al.

² exhaled breath analysis with a colorimetric sensor array for the identification and characterization of lung cancer. mazzone, p.j., et al.

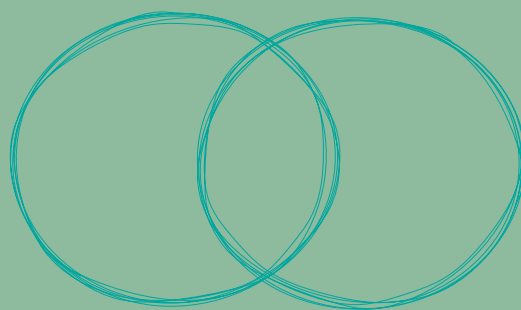
³ non-invasive breath analysis of pulmonary nodules. peled, n., et al.

⁴ exhaled breath analysis for the early detection of lung cancer: recent developments and future prospects. nardi-agmon, i., et al.

⁵ tracking the evolution of non small cell lung cancer jamal-hanjani, m., et al.

⁶ see abstract LBA1006

⁷ the potential of circulating tumor DNA [ctDNA] to guide adjuvant chemotherapy decision making in locally advanced rectal cancer [LARC]. tie j., et al.



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