Background: K and P bind different HER2 domains and have marked antitumor activity in HER2+ breast cancer. KRISTINE (NCT02131064) is an open-label phase III study comparing neoadjuvant K + P (KP) vs. TCHP in patients with HER2+ EBC. This provides the first phase III data for a complete neoadjuvant regimen omitting standard chemotherapy. Methods: The primary endpoint was pCR rate (ypT0/is, ypN0). Treatment-naïve women with stage II-IIIC centrally assessed HER2+ EBC were randomized to six cycles of KP or TCHP and were then evaluated for pCR. The Cochran Mantel-Haenszel x 2-test stratified by hormone receptor status and clinical stage was used to compare pCR rates. The study had 90% power to detect a 15% increase in pCR from 60% (TCHP) to 75% (KP). Secondary endpoints included breast conserving surgery (BCS) rate, safety, and patient-reported outcomes. Results: Baseline demographic and disease characteristics were comparable between the TCHP (n = 221) and KP (n = 223) arms. The pCR rates were 55.7% (95% CI: 48.8-62.3) and 44.4% (95% CI: 37.8-51.2) in the TCHP and KP arms, respectively (p = 0.0155). More women in the TCHP vs. KP arm underwent BCS (52.6 vs 41.7%; p = 0.0228). In patients with ER+ EBC, pCR was 44.8% in the TCHP arm and 37.9% in the KP arm; it was 72.4% with TCHP and 53.8% with KP in women with ER-EBC. The incidence of grade 3 adverse events and serious adverse events was lower with KP in the safety population (Table). Time to a 10-point decrease from baseline in health-related quality of life (HRQoL, 4.6 vs. 3.0 months) and physical function (4.9 vs. 2.8 months) was longer in the KP arm. Conclusion: While treatment with KP led to pCR in 44.4% of women, TCHP yielded a significantly higher pCR rate. However, KP had a notably better safety profile, and HRQoL and physical functioning were maintained longer. Clinical trial information: NCT02131064.
Background: The primary aim of this randomized trial of neoadjuvant therapy in operable, HER2-positive breast cancer (BC) was to determine the effect on pathologic complete response (pCR) rates of substituting lapatinib (L) for trastuzumab (T) in combination with weekly paclitaxel (WP) following adjuvant chemotherapy (AC) as well as adding L to T with WP following AC. Previously reported results showed pCR breast 52.5% for AC→WP+T, 53.2% for AC→WP+L, and 62% for AC→WP+TL. Planned secondary endpoints included five-year recurrence free interval (RFI) and overall survival (OS) and are reported here.

Methods: All patients received standard AC q3wks x 4 cycles followed by WP (80 mg/m²) on days 1, 8, and 15 q28 days x 4 cycles. Concurrently with WP, patients received either T (4 mg/kg load, then 2 mg/kg) weekly until surgery, L (1,250 mg) daily until surgery, or weekly T plus L (750 mg) daily until surgery. Following surgery, all patients received T to complete 52 wks of HER2-targeted therapy. 529 patients were randomized and 522 had follow-up. Median follow-up for this analysis was five years. Results: Five-year RFI was 84.3% for AC→WP+T, vs. 78.6% for AC→WP+L (HR: 1.27; 95% CI: 0.74-2.20; p = 0.14), and 90% for AC→WP+TL (HR: 0.66; 95% CI: 0.34-1.25; p = 0.33). Five-year OS was 94.5% for AC→WP+T, vs. 89.4% for AC→WP+L (HR: 1.52; 95% CI: 0.69-3.35; p = 0.11), and 95.7% for AC→WP+TL (HR: 0.63; 95% CI: 0.24-1.67; p = 0.55).

Conclusions: Results of five-year outcomes (RFI and OS) were consistent with previously reported findings regarding pCR status. While pCR, RFI, and OS were numerically better with the dual combination and less with L, the differences were not statistically significant. However, achievement of pCR again correlated with improved outcomes and the improvement was more remarkable in the ER-negative subset. Support: GlaxoSmithKline.

Clinical trial information: NCT00486668.
ETNA (EVALUATING TREATMENT WITH NEOADJUVANT ABRAXANE) RANDOMIZED PHASE III STUDY COMPARING NEOADJUVANT NAB-PACLITAXEL (NAB-P) VERSUS PACLITAXEL (P) BOTH FOLLOWED BY ANTHRACYCLINE REGIMENS IN WOMEN WITH HER2-NEGATIVE HIGH-RISK BREAST CANCER: A MICHELANGELO STUDY

First Author: Luca Gianni

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Background: Neoadjuvant chemotherapy regimens employing anthracyclines and taxanes have reported essentially doubled pCR rates with the addition of a taxane after anthracycline combinations. A reverse sequence did not reduce activity. Nab-paclitaxel (nab-P) is an albumin-bound nanoparticle of paclitaxel (P) that allows for safe infusion without premedication and led to a significantly higher rate of pCR in the GeparSepto trial (Untch, et al. Lancet Oncol. 2016).

Methods: This multicenter open label study (NCT01822314) in collaboration with GEICAM and BCRC-WA randomized 695 patients with centrally confirmed HER2-negative breast cancer to P 90 mg/m² (349 patients) or nab-P 125 mg/m² (346 patients). The two drugs were given on weeks 1, 2, and 3 followed by one-week rest for four cycles before four cycles of an anthracycline regimen per investigator choice.

Results: The intent to treat analysis of the primary endpoint pCR (absence of invasive cells in breast and nodes) along with the overall objective of clinical response after systemic therapy is reported below.

Conclusions: The improved rate of pCR after nab-P failed to reach statistical significance. The multivariate analysis revealed that tumor subtype was the most significant factor (OR 5.11) influencing treatment outcome. Extensive collection and banking of tumor (90%) and blood was performed and translational studies might provide clues for more informative correlations with available results. Supported in part by an unrestricted grant from Celgene.

Clinical trial information: NCT01822314.
PRELIMINARY OUTCOME OF A PRIMARY CARE-BASED SKIN CANCER SCREENING PROGRAM

First Author: Laura Ferris
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Background: Screening for melanoma has the potential to save lives through early detection. However, few studies of organized screening programs have been reported in the USA. Methods: Primary care providers (PCP) who are part of UPMC, a large healthcare system in western Pennsylvania, were offered online training in skin cancer screening (using the validated INFORMED module) and asked to provide an annual skin examination to patients aged 35 years and older who presented for routine care. Demographics of screened patients, screening rate by PCP completion of training, and depth of melanomas diagnosed in screened vs. unscreened patients for the first 12 months of this initiative are presented. Results: In 2014, 333,788 screen-eligible patients were seen at UPMC and 51,772 (15.5%) were screened for skin cancer; the remaining patients made up the unscreened cohort. Patients seen by a PCP who completed the online training were more likely to be screened (24.7% of eligible patients vs. 12.6% with a PCP who did not complete training; p = 0.001). The median age of screened patients was 60 years and the ratio of women to men screened was 1.3. Of screened individuals, 90.5% reported their race as white. Using hospital records and cancer registry data, we identified 48 incident melanomas in the screened group and 99 in the unscreened group. In the screened group, melanomas were diagnosed more frequently (one per 1,078 in the screened group vs. one per 2,849 in the unscreened group; p = 0.001), thinner (mean Breslow depth of 0.32 vs. 0.87 mm, in the unscreened group; p = 0.023), and more likely to be in situ, although this did not achieve statistical significance (39.6% in screened group vs. 28.3% in the unscreened group; p = 0.168). Conclusions: Physician education and population-based screening for melanoma results in detection of thinner melanomas. Since melanoma thickness is predictive of mortality, physician education and patient screening has the potential to reduce melanoma mortality, although further studies will be needed to confirm this. This approach also resulted in higher rates of screening of men, who are at highest risk of death from melanoma but have much lower screening rates than women, than other initiatives reported in the literature.
1546 Poster Session (Board #369)

Mon, 8:00 AM-11:30 AM

IMPACT OF ASPIRIN USE ON THE INCIDENCE OF HEAD AND NECK CANCERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

First Author: Prakash C. Neupane

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Background: In addition to its widely accepted role in cardiovascular disease, aspirin use has been associated with decreased risk of several malignancies, especially colorectal cancer. The United States Preventive Task Force has recently updated their guidelines and added colorectal cancer prevention as an added benefit to aspirin use. However, the impact of aspirin use on the risk of cancers of the head and neck cancer (HNC) has not been reviewed previously.

Methods: A systematic search of PubMed and Embase was performed to identify studies which evaluated the relationship between aspirin use and risk of HNC. Case-control studies and cohort studies were both included in the review. Random effects model was used to estimate a pooled effect size and the inconsistency index (I²) was used to estimate heterogeneity between included studies. We hypothesized that tobacco users are more likely to be prescribed aspirin and also had an increased risk for HNC and thus planned a sensitivity analysis to exclude studies which did not adjust for tobacco usage.

Results: After reviewing 879 reports, eight studies that described the association between aspirin use and HNC risk were selected, all of which were reported from Europe or North America. A total of 206,865 patients were included in six case-control studies and two cohort studies of whom 8,395 patients had HNC. Controls were matched for age and sex in all case-control studies and for tobacco use in two studies. In a meta-analysis, aspirin use reduced the risk of HNC; however, this association was of borderline statistical significance (OR: 0.87; 95% CI: 0.75-1.02). Moderate heterogeneity (I² = 50%; p = 0.05) was seen in this meta-analysis which was lost in our sensitivity analysis. On restricting meta-analysis to studies which adjusted for tobacco use (n = 7), aspirin use was found to be associated with a significantly reduced risk of HNC (OR: 0.84; 95% CI: 0.73-0.96) with low heterogeneity (I² = 35%; p = 0.16)

Conclusions: Aspirin users appear to be at lower risk for HNC after adjustment for tobacco use. Additional cohort studies are required to evaluate the optimal dose or duration of use of aspirin that may confer this protective effect.
Background: Male breast cancer (MBC) is rare. Hormones have a central role in the pathogenesis of this malignancy. The possible correlation between MBC and hormone-affecting or gynecomastia-causing medicines has been sparsely studied. Studies of men with benign prostate hyperplasia (BPH) have shown an increased risk of MBC. The aim of this study is to examine if medicines known to alter the hormonal balance or cause gynecomastia may increase the risk of contracting MBC.

Methods: Since July 2005, 369 cases of MBC were identified from the Swedish Cancer Register and each case was matched to five controls (n = 2,971) from the general population of the same age and domicile. Medicines with documented side effects of hormonal imbalance or gynecomastia were collected from the Prescribed Drug Register in operation since July 2005. Drug exposure was followed both for cases and controls until the cancer diagnosis or death of the patient. Cases and controls with a diagnosis of prostate cancer were excluded. The data were mainly analyzed with conditional logistic regression and Cox regression. Results: A reduced risk was observed among users of testosterone 5a reductase inhibitors (5-ARI) (HR: 0.41; 95% CI: 0.17-1.00). A statistically significant positive risk was observed among users of a-adrenergic receptor antagonists (aARA) (HR: 2.24; 95% CI: 1.48-3.39). Comparing 5-ARI with aARA users gave a reduced risk of MBC (HR: 0.17; 95% CI: 0.06-0.50). No other medication was significantly associated with an increased or decreased risk of MBC. Conclusions: The risk of MBC was statistically significantly higher among men using aARAs as has previously been shown for BPH. There was a decreased risk of MBC for users of 5-ARIs. This suggests that 5-ARI medication might protect against MBC. Research should therefore focus on the possible protective role of 5-ARI and investigate the increased risk of MBC among users of aARAs or BPH by itself. Men with BRCA2 mutations might be candidates for prevention with 5-ARI, and 5-ARI should be explored as a therapeutic agent in MBC and in androgen receptor-positive female breast cancer.
THE OPPORTUNITY COST (OC) OF LOW ADHERENCE WITH SCREENING (SCR) RECOMMENDATIONS FOR COLORECTAL CANCER (CRC)

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Background: Screening (Scr) rates are 60% below the Healthy People 2020 target of 70.5%, leaving 20 million people unscreened. Prior cost effectiveness analyses (CEA) have shown that although Scr is more costly compared to no Scr, the incremental cost effectiveness ratios (ICER) for Scr are favorable. However, these CEAs did not include the costs of drugs such as oxaliplatin and bevacizumab. More effective treatments and longer overall survival with advanced colorectal cancer (CRC) result in higher average societal costs of care. Methods: A Markov model was built to represent the CRC incidence and its natural history in the US general population. Individual level simulation was used to compare the benefits of CRC Scr from a societal perspective. Costs and effects were discounted (Dis) at 3%. Twelve Scr strategies (ST) were compared to no Scr. Discounted life years (LY), incidence reduction (IR), CRC mortality reduction (CMR), and discounted costs were measured. ICERs were calculated. Results: Among the STs studied, only stool DNA Scr cost more than no Scr. CS is the most effective ST and the least expensive. This represents an opportunity cost (OC) of US$ 554 per eligible individual for non-compliance with Scr and is the result of increasing costs of CRC care. With 20 million individuals at risk for preventable CRC, the OC is staggering. Conclusions: With improved survival, increasingly costly treatment regimens, and additional lines of treatment, the OC for not Scr will increase. Efforts to improve Scr adherence can result in significant societal savings by preventing the losses from OC. Strategy Comparative Effectiveness Costs Cost Effectiveness Dis LY IR CMR Cancer Care OC ($) ICER Status (Rank).
SCREENING WITH LOW-DOSE COMPUTED TOMOGRAPHY (LDCT) OF ASBESTOS-EXPOSED SUBJECTS AND LUNG CANCER (LC) MORTALITY

First Author: GianPiero Fasola
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Background: Our prospective non-randomized ATOM002 study showed that low-dose computed tomography (LDCT) screening of asbestos-exposed subjects can identify lung cancer (LC) at an earlier and potentially more curable stage than chest radiographs (CXR) (Fasola, et al. Oncologist. 2007). The ATOM002 cohort was selected from subjects enrolled in a surveillance program with annual CXR for asbestos-exposed workers at the Monfalcone Occupational Health Unit, in the Friuli Venezia Giulia (FVG) region, Italy. Here, we report a cohort mortality study of asbestos-exposed subjects from that surveillance program, comparing outcomes in the ATOM002 participants (P) and contemporary non-participants (NP).

Methods: Within a cohort of 2,433 asbestos-exposed subjects, we compared mortality between the ATOM study Ps (who had additional baseline and one-year LDCT) and NPs (n = 926 and 1,507, respectively). The follow-up period spanned the years 2002-2011. We performed Cox models to assess survival for all causes, all cancers, LC, and malignant pleural mesothelioma. Final models estimating mortality hazard ratios (HR) were adjusted for smoking habits, age, level of asbestos exposure and Charlson-Quan comorbidity index. For external comparison, we estimated the standardized mortality rate ratio (SMR) using FVG regional standard rates.

Results: There was a significant 59.3% (95% CI: 3.9-82.8) reduction in adjusted mortality for LC among ATOM002 Ps vs. NPs. The LC crude mortality was 99.4 per 100,000 person-years in Ps (eight LC deaths) compared to 430.4 per 100,000 person-years in NPs (50 LC deaths). Mortality was also reduced for all causes (HR: 0.61; 95% CI: 0.44-0.84), but not for all cancers (HR: 0.97; 95% CI: 0.62-1.50) or malignant pleural mesothelioma (HR: 0.86; 95% CI: 0.31-2.41). Compared with regional mortality rates, a trend towards reduced mortality for LC was found among ATOM study Ps (SMR: 0.55; 95% CI: 0.24-1.09), in contrast to a statistically significant increase in the NPs (SMR: 2.07; 95% CI: 1.53-2.73).

Conclusions: Participation in the LDCT screening was associated with reduced LC mortality compared to CXR-based surveillance. To our knowledge, this is the first report suggesting a reduction in mortality from LC with LDCT screening in an asbestos-exposed population.
APPLICATION OF THE 2015 AMERICAN CANCER SOCIETY SCREENING MAMMOGRAPHY GUIDELINES: RISK ASSESSMENT FOR WOMEN AGED 40-44

First Author: Jennifer Kay Pluchta
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Background: The new American Cancer Society (ACS) screening mammography guidelines suggest that only women with an above average risk require mammography screening between ages 40-44 (> 15% lifetime risk of breast cancer and/or > 5% risk of BRCA mutation). In addition, the ACS recommends yearly MRI if the lifetime risk is > 20%. We previously found that 50% of women aged 40-44 who were evaluated at an Academic breast surgery practice would be eligible for mammograms, MRI, and/or genetic testing. Here, we sought to determine these numbers at a Community breast imaging center, which we assumed would be a cohort more representative of the general population.

Methods: Under institutional review board approval, we reviewed a database from 10/1/2015 to 12/28/2015 of patient-reported risk factors and family history at a Community breast imaging center. We excluded all men, and women with a history of breast cancer. Using Tyrer Cuzick, Claus, or BRCAPRO, those with a > 15% lifetime risk of breast cancer or > 5% risk of BRCA mutation (eligible for genetic testing) were considered above average risk. Those with a > 20% lifetime risk were also eligible for screening MRI. We assessed these results in Jewish and non-Jewish women.

Results: 7,357 women age > 40 years without breast cancer were evaluated. Of these, 909 (12.4%) were aged 40-44 and constitute our cohort. Risk assessment identified 485 women (53.4%) who were eligible for mammography. Conclusions: At this Community breast imaging center, 53.4% of women aged 40-44 would have been eligible for screening mammography. These numbers were higher in Jewish women. Thus, it is critical that women aged 40-44 have formal risk assessment in order to identify those who would qualify for screening mammography, screening MRI, and genetic testing.

Non-Jewish n = 806 (89%); Jewish n = 103 (11%); Total n = 909 (100%).
All mammography: 410 (50.9%), 75 (72.8%), 485 (53.4%).
Mammography, no MRI or genetic testing: 169 (21%), 29 (28.2%), 198 (21.8%).
Mammography + MRI, no genetic testing: 176 (21.8%), 12 (11.7%), 188 (20.7%).
Mammography + MRI + genetic testing: 38 (4.7%), 24 (23.3%), 62 (6.8%).
Mammography + genetic testing, no MRI: 27 (3.3%), 10 (9.7%), 37 (4.1%).
USE AND ADHERENCE TO BREAST CANCER RISK-REDUCTION AGENTS:
A POPULATION-BASED STUDY

FIRST AUTHOR: MARINA CHAVEZ-MAC GREGOR
The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: Tamoxifen, raloxifene, and aromatase inhibitors (AI) reduce the risk of developing breast cancer (BC). Risk-reduction agents are recommended for women at high risk of BC defined as a five-year risk > 1.7% using the Gail model or age > 60. We describe the use of risk-reduction agents, adherence rates, and determinants of adherence among women aged > 60.

Methods: Market scan participants aged > 60, with claims between 2008-2013 and 18 months of continuous coverage were identified. Women with ductal carcinoma in situ, lobular carcinoma in situ, or any invasive cancer diagnosis were excluded. Prescriptions for risk-reduction agents were identified; however, raloxifene claims linked to an osteoporosis diagnosis were excluded. Descriptive Statistics and multivariable regression models were used. Among participants initiating therapy with risk-reduction agents, adherence was evaluated measuring the proportion of days covered (PDC) in 12 continuous months. Adherence was defined as PDC > 80%.

Results: Among 3,398,001 women, 61,329 (1.8%) used risk-reduction agents. Determinants of use included older age (OR: 1.34; 95% CI: 1.31-1.37) and residence in the north-central (OR: 1.61; 95% CI: 1.57-1.65), and south (OR: 1.5; 95% CI: 1.46-1.54) regions of the USA. High comorbidity score (OR: 0.59; 95% CI: 0.5-0.58), living in areas with the lowest income (OR: 0.92; 95% CI: 0.9-0.95) or—as a proxy for race—high proportion of African Americans (OR: 0.87; 95% CI: 0.84-0.89) and Hispanics (OR: 0.82; 95% CI: 0.79-0.84) were associated with decreased use. Adherence was evaluated in 12,026 women, of whom 37.4% had a PDC > 80%. Factors associated with adherence included 90 rather than 30 day prescription (OR: 2.66; 95% CI: 2.43-2.91), and tamoxifen (OR: 1.36; 95% CI: 1.03-1.79) or AI (OR: 1.72; 95% CI: 1.42-2.1) use compared to raloxifene. Residence in areas with high proportion of African Americans (OR: 0.87; 95% CI: 0.76-0.99) and higher out-of-pocket cost (OR: 0.89; 95% CI: 0.82-0.97) were associated with poor adherence.

Conclusions: A very small proportion of insured women aged > 60 are prescribed risk-reduction agents. Among those receiving treatment, adherence is low. Prescription-related factors and sociodemographic characteristics are associated with use and adherence indicating potential areas for intervention.
RETHINKING THE HISPANIC ADVANTAGE IN CANCER OUTCOMES: INFLUENCE OF BIRTHPLACE

First Author: Paulo Pinheiro

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Background: In the USA, the Hispanic advantage in cancer outcomes over non-Hispanic Whites (NHW) derives from studies aggregating heterogeneous Hispanic subgroups and ignoring birthplace. Here, for the first time, we provide a detailed analysis of cancer mortality by birthplace for the largest Hispanic subgroup, Mexican Hispanic (MH), which comprises 65% of all US Hispanics. Methods: Cancer-specific mortality rates, age adjusted to the 2000 US standard population, were calculated for NHW, US-born Mexican Hispanic (USB-MH) and Mexican-born Mexican Hispanic (MB-MH) residents of California. Age-adjusted mortality ratios obtained from Poisson regression models were used to compare rates. Results: 283,052 cancer deaths from 2008-2012 were analyzed, including 185,840 in NHW, 17,978 in USB-MH, and 18,593 in MB-MH. The NHW males had the highest all cancers-combined mortality rates (201 per 100,000), followed by USB-MH and MB-MH (191 and 131 per 100,000, respectively). Rates for females were 152 for NHW, 125 for USB-MH, and 96 for MB-MH per 100,000. Overall risk of cancer death was 1.57 and 1.49 times higher for NHW and USB-MH than MB-MH (p = 0.01). For liver and colorectal cancer, USB-MH males had a risk 2.48 and 1.82 times higher than NHW, and 2.85 and 1.30 times higher than MB-MH (p = 0.01). Conclusions: Assumptions about the relative advantage of Hispanic ethnicity for cancer outcomes need to be reexamined. Mexican Hispanic populations born in the USA have an increased risk of mortality compared to those born in Mexico; their overall risk of cancer mortality approaches that of NHW. The prototypical advantage of Hispanics (low smoking prevalence and low lung cancer rates) is counterbalanced by increases in mortality for most cancers; for males, the increases in liver and colorectal cancers are substantial. This bolsters evidence of a first-generation Healthy Immigrant Effect, rather than an ethnicity-specific benefit for Hispanics. Crucial to cancer prevention and control efforts is the identification of factors that can halt this unfavorable convergence of rates from lower to higher risk among the largest growing minority population in the USA: Hispanics.