Results: Results across the cohort indicate Her2 MRM results correlate precisely with IHC and FISH demonstrating Her2 quantitation in Liquid Tissue lysates obtained by microdissecting multiple cancerous regions across the same tissue section and processing them together to produce a single lysate. Results of this assay across different regions within the same tumor tissue indicate different levels of Her2 are detected in different cancerous and stromal regions within the same tissue section that correlate precisely with IHC analysis in these various regions.
Conclusion: These results indicate the need for a sampling strategy for measuring quantitative levels of specific proteins directly in patient tissue that requires tissue microdissection with implications for the molecular analysis of tumor tissue for advanced diagnostic applications.

PP116

Lycopene and prostate cancer

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Background: The purpose of this Phase II randomized-controlled trial was to evaluate the safety and effect of administering several doses of lycopene to men with clinically localized prostate cancer, on intermediate endpoint biomarkers implicated in prostate carcinogenesis.
Materials and Methods: Forty-five eligible men with clinically localized prostate cancer were supplemented with 15, 30 or 45 mg of lycopene or no supplement from biopsy to prostatectomy. Compliance to study agent, toxicity, changes in plasma lycopene, serum steroid hormones, PSA and tissue Ki-67 were analyzed from baseline to completion of intervention
Results: Forty-two of forty-five five subjects completed the intervention for approximately 30 days from the time of biopsy until prostatectomy. Plasma lycopene increased from baseline to post treatment in all treatment groups with greatest increase observed in the 45 mg lycopene-supplemented arm compared to the control arm without producing any toxicity. Overall, subjects with prostate cancer had lower baseline levels of plasma lycopene similar to those observed in previous studies in men with prostate cancer. Serum free testosterone decreased with 30 mg lycopene supplementation and total estradiol increased significantly with 30 mg and 45 mg supplementation from baseline to end of treatment, with no significant increases in serum PSA or tissue Ki-67. These changes were not significant compared to the control arm for this sample size and duration of intervention.
Conclusion: Although antioxidant properties of lycopene have been hypothesized to be primarily responsible for its beneficial effects, our study suggests that other mechanisms mediated by steroid hormones may also be involved

PP60

Correlation of absolute lymphocyte count with clinical benefit and overall survival: results of compassionate-use trial of ipilimumab in advanced melanoma at Memorial Sloan-Kettering Cancer Center

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Background: Ipilimumab (ipi) is a monoclonal antibody which antagonizes cytotoxic T lymphocyte antigen (CTLA)-4, a negative regulator of the immune system. We report on advanced refractory melanoma Pts treated on a trial of compassionate-use ipi at the Memorial Sloan-Kettering Cancer Center.
Materials and Methods: Eligibility criteria included stage III (unresectable) or stage IV melanoma. Pts had experienced progressive disease to at least one prior systemic therapy (except for those with ocular primary tumors, who were required to have local control of their disease). Pts with primary ocular or mucosal melanomas were eligible, as were those with brain metastases. Pts received ipi 10 mg/kg every three weeks for four induction doses. Those Pts with evidence of clinical benefit (CB) at Week 24 − complete or partial response (CR or PR) or stable disease (SD) as defined by modified WHO criteria − then received maintenance ipi every 12 weeks.
Results: 53 Pts were enrolled, with 51 evaluable (one was lost to follow-up after one ipi treatment while the other received chemotherapy between ipi treatments). The median age of Pts was 62 years (range, 38−86 years). 64% of Pts were male and most had an excellent performance status (85% with ECOG status 0−1). 25% of Pts had an abnormally elevated lactate dehydrogenase (LDH) level $\leqslant 2\times$ the upper limit of normal (ULN) and 32% had a baseline LDH $> 2 \times$ ULN. Grade 3/4 immune-related adverse events (irAEs) were noted in 29% of Pts, with the most common irAEs being pruritus (43%), rash (37%) and diarrhea (33%). The response rate (CR+PR) was 12% (95% CI: 5%, 25%) while 29% had SD (95% CI: 18%, 44%). Median progression-free survival was 2.5 months while median overall survival (OS) was 7.2 months (95% CI: 4.0, 13.3). Pts with grade 3/4 irAEs appeared to have improved Week 24 CB rate. Pts with an absolute lymphocyte count (ALC) $\geqslant$1,000/μL (33/41 Pts) after two ipi treatments (week 7) had significantly improved CB rate (45% versus 0%, $p = 0.02$) and median OS (11.9 versus 1.4 months, $p < 0.001$) compared to those with an ALC < 1,000/μL (8/41 Pts). Six and 12 month OS were 75% vs. 0% and 47% vs. 0% when stratified by Week 7 ALC. This association remained significant when controlled for baseline LDH level.
Conclusion: Our results confirm that ipi is clinically active in Pts with advanced refractory melanoma. The ALC after two ipi treatments appears to strongly correlate with CB and OS and should be prospectively validated.

PP52

Amplification of the chromosome 17 q22 amplicon containing TOP2A gene is correlated with better survival in HER2 amplified/ hormone receptors negative breast cancers

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Background: HER2 amplified breast cancers are considered as a homogeneous sub-group of breast cancers. It has been described that amplifications in the chromosome 17 (ch17) could affect different genes implicated in cancer development. The aim of the study was to determine, by quantitative PCR, the levels of amplification of different genes located on ch17q (on the centromeric side and distal side of the chromosome in regards of HER2 localization), and their relation with patient's survival.
Materials and Methods: We determined MED1 (centromeric side) and TOP2A IGFBP4, CCR7, KRT20, KRT19 and GAS (distal side) gene copy numbers by quantitative PCR in 87 HER2 amplified breast tumors. Patients were included between 2002 and 2006 (median follow-up = 40.3 month). They received radiotherapy (100%), anthracyclin based regimen (78%), taxanes (2%), herceptin (24%) and hormonotherapy (40%) as adjuvant therapy according to therapeutic recommandations used at the time of surgery.
Results: Gene amplification occurs in 65.6% for MED1 (57/87), 23% for TOP2A (22/65), 19.5% for IGFBP4 (17/87), 18.4% for CCR7 (16/87), 13.8% for KRT20 (12/87), 11.5% for KRT19 (10/87), and 6.9% for GAS (6/87). The level of amplification of HER2 is correlated with the level of amplification of MED1 ($p < 0.0001$) but not with others gene amplification's levels. HER2-MED1 amplicon is associated mostly with hormone receptors positive breast tumor ($p < 0.01$). Hormone receptors negative patients have the worst overall survival (OS) (HR 0.356; 95% CI 0.16−0.783; $p < 0.01$), median progression-free survival (PFS) after recurrence was 36.5 compare to 43 months for positive hormone receptors patients. In hormone negative patients, amplifications of HER 2 +/− MED1 genes have a worse OS (HR 0.277; 95% CI 0.131−0.588; $p < 0.0008$) than patient with amplification of genes located on the distal side; PFS after recurrence was 35 compared to 43 months, respectively.
Conclusion: HER2 and MED1 are located on the same amplicons. The Amplification of genes located on the distal side of ch17 determines a profile with a better survival in hormone receptors negative breast cancer. This could be explained by a better response to anthracyclin based regimen for hormone-independent -TOP2A amplified breast cancer.

PP114

Non-coding mitochondrial RNA differential expression: a new biomarker for noninvasive cancer diagnosis

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Background: Recently, we described the existence in human cells of a family of non-coding mitochondrial RNAs (ncmtRNAs) formed by the sense or antisense 16S mitochondrial rRNA, and an inverted repeat (IR) of variable size covalently linked to its 5′ end. These transcripts were named sense ncmtRNA (SncmtRNA) and antisense ncmtRNA (ASncmtRNA) respectively. The expression of these transcripts varies depending of the proliferative status of the cell. In resting cells, the sense and antisense transcripts are down-regulated. In normal proliferating cells, both transcripts are highly represented. In tumor cells, however, only the antisense transcript is selectively repressed. Based on the universal representation and the differential expression of these ncmtRNAs, the goal of this research is to demonstrate the enormous potential in cancer diagnostic of these molecules and their use as a new biomarker in human neoplasias. By double in situ fluorescent hybridization (FISH), we are developing a non invasive approach for the diagnosis of prostate and bladder cancer