

**RESULTS:** Generally, patients had high expectations that they would benefit from GTT ( $M = 2.81$  on 0-4 scale) and positive attitudes toward it ( $M = 2.98$  on 0-4 scale). Patients also had relatively poor knowledge about GTT (48% correct answers on an objective test of GTT knowledge). Greater expectations for GTT were associated with lower knowledge ( $b = -0.46$ ;  $p < .001$ ), more positive attitudes ( $b = 0.40$ ;  $< .001$ ), and lower education ( $b = -0.53$ ;  $< .001$ ). **DISCUSSION/SIGNIFICANCE:** This research suggests patients have high expectations that they will benefit from GTT, which is associated with low knowledge, positive attitudes, and low education. Interventions may be needed to boost understanding and moderate expectations, particularly for disadvantaged patients.

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### MYC Inhibition Overcomes IMiD Resistance in Heterogeneous Multiple Myeloma Populations<sup>†</sup>

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**OBJECTIVES/GOALS:** Immunomodulatory drugs (IMiDs) are critical to multiple myeloma (MM) disease control. IMiDs act by inducing Cereblon-dependent degradation of IKZF1 and IKZF3, which leads to IRF4 and MYC downregulation (collectively termed the "Ikaros axis"). We therefore hypothesized that IMiD treatment fails to downregulate the Ikaros axis in IMiD resistant MM. **METHODS/STUDY POPULATION:** To measure IMiD-induced Ikaros axis downregulation, we designed an intracellular flow cytometry assay that measured relative protein levels of IKZF1, IKZF3, IRF4 and MYC in MM cells following ex vivo treatment with the IMiD Pomalidomide (Pom). We established this assay using Pom-sensitive parental and dose-escalated Pom-resistant MM cell lines before assessing Ikaros axis downregulation in CD38+CD138+ MM cells in patient samples (bone marrow aspirates). To assess the Ikaros axis in the context of MM intratumoral heterogeneity, we used a 35-marker mass cytometry panel to simultaneously characterize MM subpopulations in patient samples. Lastly, we determined ex vivo drug sensitivity in patient samples via flow cytometry. **RESULTS/ANTICIPATED RESULTS:** Our hypothesis was supported in MM cell lines, as resistant lines showed no IMiD-induced decrease in any Ikaros axis proteins. However, when assessed in patient samples, Pom treatment caused a significant decrease in IKZF1, IKZF3 and IRF4 regardless of IMiD sensitivity. Mass cytometry in patient samples revealed that individual Ikaros axis proteins were differentially expressed between subpopulations. When correlating this with ex vivo Pom sensitivity of MM subpopulations, we observed that low IKZF1 and IKZF3 corresponded to Pom resistance. Interestingly, most of these resistant populations still expressed MYC. We therefore assessed whether IMiD resistant MM was MYC dependent by treating with MYCi975. In 88% (7/8) of patient samples tested, IMiD resistant MM cells were sensitive to MYC inhibition. **DISCUSSION/SIGNIFICANCE:** While our findings did not support our initial hypothesis, our data suggest a mechanism where MYC expression becomes Ikaros axis independent to drive IMiD resistance, and resistant MM is still dependent on MYC. This suggests targeting MYC directly or indirectly via a mechanism to be determined may be an effective strategy to eradicate IMiD resistant MM.

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### Transcriptomics for gallbladder cancer prognosis

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**OBJECTIVES/GOALS:** Recent research has attempted to identify diagnostic, prognostic, and predictive biomarkers, however, currently, no biomarkers can accurately diagnose GBC and predict patients prognosis. Using machine learning, we can utilize high-throughput RNA sequencing with clinicopathologic data to develop a predictive tool for GBC prognosis. **METHODS/STUDY POPULATION:** Current predictive models for GBC outcomes often utilize clinical data only. We aim to build a superior algorithm to predict overall survival in GBC patients with advanced disease, using machine learning approaches to prioritize biomarkers for GBC prognosis. We have identified over 80 fresh frozen GBC tissue samples from Rochester, Minnesota, Daegu, Korea, Vilnius, Lithuania, and Calgary, Canada. We will perform next-generation RNA sequencing on these tissue samples. The patients clinical, pathologic and survival data will be abstracted from the medical record. Random forests, support vector machines, and gradient boosting machines will be applied to train the data. Standard 5-fold cross validation will be used to assess performance of each ML algorithm. **RESULTS/ANTICIPATED RESULTS:** Our preliminary analysis of next generation RNA sequencing from 18 GBC tissue samples identified recurrent mutations in genes enriched in pathways in cytoskeletal signaling, cell organization, cell movement, extracellular matrix interaction, growth, and proliferation. The top three most significantly altered pathways, actin cytoskeleton signaling, hepatic fibrosis/hepatic stellate cell activation, and epithelial adherens junction signaling, emphasized a molecular metastatic and invasive fingerprint in our patient cohort. This molecular fingerprint is consistent with the previous knowledge of the highly metastatic nature of gallbladder tumors and is also manifested physiologically in the patient cohort. **DISCUSSION/SIGNIFICANCE:** Integrative analysis of molecular and clinical characterization of GBC has not been fully established, and minimal improvement has been made to the survival of these patients. If overall survival can be better predicted, we can gain a greater understanding of key biomarkers driving the tumor phenotype.

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### Rib Fractures in Geriatric Trauma: A Review of 1,037 Cases at a Single Level I Trauma Center

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**OBJECTIVES/GOALS:** Rib fractures are common traumatic thoracic injuries and are associated with high rates of morbidity and mortality. In those age  $\geq 65$ , the rate of these complications double. This study sought to identify the extent to which injury-related predictors influence