Abstracts

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Serum infliximab and corresponding anti-infliximab antibody: Analysis of over 30,000 patient results using lab developed chemiluminescent immunoassays

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BACKGROUND: Assays to measure TNF inhibitors and anti-drug antibodies (ADAb) in patient serum are being utilized to manage failure to respond and loss of response. Monitoring assays may also be used to proactively titrate doses and dosing intervals (1). Here, 37,165 infliximab (IFX) patient results over 4 years were analyzed.

METHODS: Measurements of drug and ADAb levels were performed by lab developed chemiluminescent immunoassays (2). The lower limits of quantitation are 0.4 ng/mL for IFX and 22 ng/mL for its ADAb. Drug assays measure free (ADAb-unbound) drug while ADAb assays detect total antibodies (including IgG and IgG subclasses) and are drug- tolerant to the presence of up to ~50 µg/mL of drug. Clinical histories and blood collection time are unknown.

RESULTS: Of 37,165 measured IFX samples, 55% (20,339) were ADAb-free and 45% (16,806) had measurable anti-infliximab antibodies, ranging in concentration from 22 to 3.5 million ng/mL. In the absence of ADAb, IFX concentrations were from 0.4 to >50 µg/mL, with the majority (>60%) between 3.0 to 20 µg/mL. In the presence of ADAb, an inverse relationship between IFX concentrations and anti-IFX antibodies was demonstrated. As a baseline reference, an ADAb-free mean drug level from lab derived samples with IFX between 0.3 and 30 ng/mL was found to be 10.0 µg/mL. Mean IFX concentrations decreased in samples with increasing ADAb. Low ADAb (<200 ng/mL) appears to have minimal impact on mean drug levels while high ADAb (>1,000 ng/mL) is invariably associated with severely diminished IFX (10% or less than the mean).

CONCLUSION(S): Upon analysis of 37,165 infliximab patient samples, 45% exhibited anti-infliximab antibodies. Though collection timing and clinical histories are not known, we found that of all ADAb-free samples, about one third (38%) were within the target range of 3–30 µg/mL for infliximab and 36% of samples were subtherapeutic at <3.0 µg/mL. High titer ADAb are almost invariably associated with very low or absent IFX levels. In contrast, low titer antibodies have little or no impact on drug levels. Further study is needed with American Gastroenterological Association Critical Care Pathways for Crohn’s Disease and Ulcerative Colitis where low and high antibody scenarios are managed very differently (increase drug dose/consider immunomodulatory vs switch within class). It may be possible to treat away low titer ADAb by increasing drug or adding an immunomodulator (3). Therefore, drug-tolerant anti-drug antibody assays that have been designed both (1) to detect low level ADAb and (2) to distinguish low to intermediate to high titer with high resolution (from 22 to 2,000 ng/mL) may be most helpful in preventing, managing and treating immunogenicity.

REFERENCES

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Potential cost avoidance benefits of the early identification of and differentiation Between IBD and IBS

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BACKGROUND: Changes in distribution and composition of microbiome species may be associated with inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). IBD, which includes ulcerative colitis (UC) and Crohn’s disease (CD) is an immune-mediated inflammatory disease. IBS is a chronic functional disease characterized by a series of symptoms such as cramping, diarrhea, and constipation. There are specific medications for IBD used to treat the underlying disease and keep it in remission, whereas IBS is more commonly addressed by treating the symptoms and adjusting one’s lifestyle to avoid triggers of the condition. Thus, distinguishing between these 2 conditions is important. To address this need,ibome has developed SmartGutTM, a sequencing-based clinical microbial test that can detect beneficial and pathogenic microorganisms associated with IBS and IBD and help distinguish between these conditions. In this study we developed a model to estimate the cost impact of using SmartGutTM in a US population of patients with gastrointestinal distress.

METHODS: A model was developed from the perspective of a US payer that provides SmartGutTM as a screening tool for beneficiaries. The model estimates the incidence of gastrointestinal distress from the combined incidence rates of IBD, IBS, and other causes. Utilization was informed by manufacturer patient analysis. The cost of SmartGutTM was based on test costs from the manufacturer.

RESULTS: For a hypothetical US payer covering 1,000,000 lives, the annual incidence of patients with chronic gastrointestinal distress is estimated to be 68,820 215,820, of which 27% are expected to receive pair testing with an average of 2.35 SmartGutTM screenings per patient for a total of 39,905 annual screenings. This costs the plan $48,318,761 annually, equating to an additional $4.03 per member per month compared to usual care. However, the SmartGutTM test report details the presence and quantity of microorganisms associated with IBS and IBD. The report includes recommendations for healthcare providers on treatment, lifestyle, and diet that can be discussed with the patient. Testing in these patients may lead to earlier identification of IBS or IBD, which may result in improved downstream outcomes and more efficient use of healthcare resources. Further research is being conducted in order to clearly delineate the test specifications of IBS and IBD as well as downstream health outcomes.

CONCLUSION(S): Here we present our initial investigations to estimate the cost avoidance benefits of early identification and differentiation between inflammatory bowel disease and irritable bowel syndrome using SmartGutTM in a US population of patients, highlighting test costs and improved outcomes.

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Is the thickness of the posas muscle a maker of poor prognosis in Crohn’s disease?

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INTRODUCTION: Recent studies point to an association between body composition and clinical outcomes in Crohn’s disease (CD).

OBJECTIVE: To determine the relationship between posas muscle thickness (PSOAs) as a marker of nutritional status and the prognosis of patients with CD.

METHODS: Retrospective study, including patients with CD who underwent computed tomography (CT) at diagnosis and with a minimum follow-up of 1 year. The axial (AT) and transverse (TT) thickness of the right PSOAs was measured at the cross-sectional level of L3-L4. AT corresponds to the maximum diameter of the PSOAs on the axial axis. TT corresponds to the diameter of the PSOAs perpendicular to the axial axis. The thickness was normalized for height. Poor prognosis was defined as the need for surgery and/or introduction of immunosuppressive therapy and/or development of perianal disease and/or altered disease behavior.

RESULTS: Included 104 patients, 62 (59.6%) female with a mean age at diagnosis of 33.9 ± 12.7 years. Patients were submitted to surgery in 37.3%. We observed a behavior change in 15.4%, development of perianal disease in 22.1% and introduction of immunosuppressive therapy in 76.9%. We found that patients who underwent surgery had lower values of AT (25.23 vs 26.78 mm/m, P = 0.024) and TT (18.70 vs 20.69 mm/m, P = 0.008). The same was observed in patients who presented change in the disease behavior of AT (24.44 vs 26.51 mm/m, P = 0.024) and TT (17.43 vs 20.40 mm/m, P = 0.003).

CONCLUSIONS: We identified that patients submitted to surgery or with behavior change had lower values of AT and TT at diagnosis. These parameters may identify patients with CD who may progress with worse prognosis, and constitute an extra tool in monitoring patients with CD.

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Ulcerative colitis: Risk factors for relapse in clinical remission patients

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BACKGROUND: Ulcerative colitis (UC) is a chronic inflammatory bowel disease, characterized by periods of remission and relapse. The aim of this study was to identify factors associated with a higher risk of relapse in patients in clinical remission.

METHODS: Retrospective study, including UC patients in clinical remission with minimum follow up of 2 years. Clinical relapse was defined as a need for therapeutic escalation and UC-related hospitalization or surgery. Statistical analysis was carried out by means of t-test and chi square (univariate analysis) and logistic regression (multivariate analysis). A P value <.05 was considered statistically significant.

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