France). These assays measure free drug and anti-drug antibody (ADAb) and therefore inhibition studies were performed on samples with detectable drug levels (>1 ug/ml) and positive ADAb. Results were classified according to drug levels (DL) and ADAb status.

Results The laboratory analysed 2424 (17% internal) samples for IFX (Median DL 3.8 ug/mL, IQR 1.2–6.3) and 1335 (21% internal) samples for ADAL (Median DL 5.2 ug/mL, IQR 3.4–7.3) from IBD patients. Prevalence of detectable antibodies was higher in IFX (10%) than ADAL (4.1%) samples. External requests originated from >90 different hospitals. Number of requests received for both assays doubled from 2013 to 2014 with batch frequency consequently decreasing from fortnightly to weekly.

Abstract PTH-090 Table 1

	Therapeutic DL (>2 ug/mL)	Intermediate DL (1.0–2.0 ug/mL)	Subtherapeutic DL (<1 ug/mL)
Infliximab	1614 (67%)	249 (10%)	561 (23%)
Anti-Infliximab antibody positive (>10 ng/mL)	0	0	245 (44%)
	Therapeutic DL (>5 ug/mL)		Subtherapeutic DL (<5 ug/mL)
Adalimumab	691 (52%)		644 (48%)
Anti-Adalimumab antibody positive (>10 ng/mL)	0		53 (8%)

40 patients had IFX >1 ug/ml and were antibody positive. 16 of these patients were confirmed to have switched to ADAL due to loss of response to IFX therapy. Detectable DL observed in these cases was due to cross reactivity of ADAL with the IFX assay. 11 patients had false positive drug levels and 4 patients had borderline antibodies due to non specific binding. 1 patient had sample collected around infusion.

4 patients had subtherapeutic ADAL (1.1–1.4 ug/ml) and were antibody positive. 1 of these patients was confirmed to have switched to IFX due to loss of response to ADAL therapy. Detectable DL observed in this case was due to cross reactivity of IFX with the ADAL assay. 3 patients had false positive results for ADAL.

From the data, it was evident that some centres monitored patients with serial measurements and made subsequent changes to therapy. 63 patients (IFX) and 52 patients (ADAL) had an average of 7 and 3 repeat measurements taken respectively.

Conclusion Anti-TNF testing has been embedded in several IBD centres as a way of optimising therapy however variation in TDM practices was observed highlighting the need for national guidance. Significant increase in test requesting suggests assay based treatment strategies combined with clinical assessment is now an accepted practice in IBD.

Disclosure of interest Z. Arkir: None Declared, N. Unsworth: None Declared, G. Richards: None Declared, Z. Odho: None Declared, P. Irving Speaker Bureau of: MSD, Abbvie and Takeda.

PTH-091 MEASUREMENT OF TNF-ALPHA DRUG LEVELS AND FREE VERSUS TOTAL ANTI-DRUG ANTIBODIES USING THREE COMMERCIALLY AVAILABLE ASSAYS

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10.1136/gutjnl-2015-309861.979

Introduction Commercial assays are now available for therapeutic drug monitoring (TDM) of anti-TNF drugs and antibodies (ADAb). Utility of free versus total ADAb assays remains debatable, further complicated by lack of assay standardisation. Here we report analytical comparison of 3 commercially available assays for Infliximab (IFX) and Adalimumab (ADAL) drug levels (DL) and ADAb.

Method Prospective evaluation of IFX and ADAL DL and ADAb was performed using our local LISA-TRACKER (LT) assay automated on e-Robot in IBD patients. Samples were also analysed by Immundiagnostik (IM, Germany) and Promonitor (PM, Spain) ELISA automated on Grifols Triturus. LT and PM utilises a specific bridging ELISA to quantitatively measure free-ADAb whereas IM utilises a dissociation step to enable detection of total-ADAb generating semi-quantitative results. IFX assays measure free drug but differ in microtitre plate coating and secondary detection reagents. Data was analysed using Passing Bablok and bias plots. LT and PM kits were provided at no cost.

Results

Summary of DL comparisons shown below:

Abstract PTH-091 Table 1

Infliximab range: 1.30 – 16.70 ug/mL	Immundiagnostik (n = 76)		Promonitor (n = 63)	
	Passing Bablok	Bias	Passing Bablok	Bias
Lisa-Tracker	IM=1.24–0.38	8.00%	PM=1.16LT – 0.43	–1.71%
Immundiagnostik			IM= 0.94PM-0.15	–4.82%
Adalimumab	(n = 78)		(n = 58)	
range: 0.2–19.9 ug/mL				
Lisa-Tracker	IM=1.73LT-0.06	79.60%	PM=1.47LT+1.25	74.00%
Immundiagnostik			IM=0.84PM+1.27	–0.30%

Samples analysed in different batches showed different kit biases against each other for IFX. Batch 1 showed that LT assay had 43.9% positive bias against ID kit whereas batch 2 demonstrated –26% negative bias. Both LT and ID kits used had different lot numbers. This change in bias was not observed in ADAL assays which showed consistent and systematic bias. PM kit showed concentration dependent bias changes within the same assay.

4 patients tested (n = 79) IFX ADAb positive with undectable DL with one exception where total/free ADAb was negative using ID and PM assays. A further 17 patients tested total ADAb positive using IM with detectable DL (0.5–9.2 ug/mL). 1 patient tested ADAL ADAb positive using LT, PM and ID assays however ID and PM assays produced positive resuts on a further 4 specimens, all with ADAL DL >5 ug/mL.

Conclusion Although commercial assays are now available, our data highlights the need for assay standardisation. Free ADAb

assays were in agreement however ADAb positivity was higher using ID assay. Significance of total ADAb positivity is unknown. Results for both IFX and ADAL confirm that DL are not transferable from one assay to another and as such, common therapeutic cut-offs will not be applicable. Further work is warranted to establish the cause of batch-to-batch variation observed.
Disclosure of interest Z. Arkir: None Declared, N. Unsworth: None Declared, B. Warner: None Declared, G. Richards: None Declared, P. Irving Speaker Bureau of: MSD, Abbvie and Takeda.

Liver – Basic Science

PTH-092 DISCOVERY AND QUANTITATION OF NOVEL LIVER FIBROSIS BIOMARKERS USING PROTEOMICS

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10.1136/gutjnl-2015-309861.980

Introduction Liver biopsy is the reference standard for assessing liver fibrosis and serum biomarkers can be used as a less invasive approach. Various antibody-based assays for serum biomarkers are currently in use to help diagnose fibrosis stage. However, these immunoassays have potential disadvantages such as the inability to detect degraded proteins and often these assays are time consuming. We have developed an antibody-free method to detect and quantify novel liver fibrosis biomarkers in human plasma/serum which overcomes these disadvantages.
Method Novel liver fibrosis biomarkers were identified by analysing proteins in plasma/serum samples from controls and patients with varying stages of liver fibrosis using a proteomics technique: two dimensional gel electrophoresis (2DE). For the most promising liver fibrosis biomarkers, an antibody-free assay (parallel reaction monitoring using mass spectrometry) was used which detects tryptic peptides of the biomarkers and their fragments. A calibration curve, established from known amounts of synthetic isotopically labelled peptides, was used to determine the concentrations of our biomarkers in serum/plasma samples from patients with varying stages of liver fibrosis.
Results Several candidate biomarkers for hepatic fibrosis were identified using 2DE. Our best biomarkers were promising when compared by Western blotting to the proteins used in existing serum biomarker tests for liver fibrosis. Using parallel reaction monitoring, antibody-free assays were developed for our most promising biomarkers which were able to successfully discriminate between neighbouring stages of liver fibrosis.
Conclusion We have developed a fast, sensitive and robust antibody-free method to detect and quantify novel liver fibrosis biomarkers in human plasma/serum. Unlike immunoassays which are restricted on the number of biomarkers due to antibody cost, our method can successfully detect and quantify more than 50 biomarkers in a single 30 min run. This novel assay may help clinicians to assess hepatic fibrosis and reduce the need for invasive liver biopsies.
Disclosure of interest None Declared.

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PTH-093 ONE YEAR MORTALITY OUTCOMES OF PATIENTS WITH LIVER CIRRHOSIS ADMITTED TO A TEACHING HOSPITAL INTENSIVE CARE UNIT

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10.1136/gutjnl-2015-309861.981

Introduction Cirrhotic patients admitted to the intensive care unit (ICU) are reported to have poor outcomes with published one year mortality rates of up to 81%.[1] ICU mortality in cirrhotic patients has improved over recent years, but there is no recent data on one year outcomes. The aim of this study was to examine one year mortality, assess organ and liver scoring systems predictive value for one year mortality and to compare outcomes in patients with alcohol and non-alcohol related cirrhosis admitted to the ICU of a non-transplant tertiary Hepatology centre.
Method This was a retrospective analysis of prospectively collected data on outcomes of consecutively admitted patients with liver cirrhosis to the Royal London Hospital, from Intensive Care National Audit and Research Centre records.
Results Between 01/01/2006 and 31/12/2013, 253 cirrhotic patients were admitted to ICU. The most common reasons for admission were sepsis (33%), GI bleed (24%) and hepatic encephalopathy (11%). Aetiologies of cirrhosis included alcohol (68%), viral hepatitis (17%) and NASH (4%). There were significant differences in median age (53 vs 57), ethnicity (White/Black/Asian – 87/5/8% vs 56/13/31%) and admissions for sepsis (38% vs 21%) between those with alcohol and non-alcohol related aetiologies. One year, hospital and ICU mortality were 66%, 57% and 39% overall, 66%, 58% and 40% in alcohol, and 66%, 54% and 38% in non-alcohol aetiologies of cirrhosis respectively (p=ns.). 1 year mortality in patients requiring 1, 2, 3 and 4 organ support was 49%, 68%, 95% and 88%. Patients requiring renal replacement therapy (RRT) had more organs failing (3 vs 1 $p < 0.0001$) and a higher MELD score (19 vs 15 $p < 0.005$) compared to those not requiring RRT. ICU, hospital and one-year mortality was 70%, 86% and 89% in this group.

Abstract PTH-093 Table 1

Predictors of one-year mortality	
Score	AUC
RIFLE	0.660
MELD	0.654
APACHEII	0.708
SAPSII	0.732
SOFA	0.707

The SAPS II score was a better predictor of one-year mortality than other organ failure scores.
Conclusion One-year mortality in our series compares favourably with the 81% previously reported in a UK transplant