Background and Aims Splanchnic vein thrombosis can lead to portal hypertension and/or bowel ischaemia with potential infarction. These complications are not always prevented by anticoagulation (Low Molecular Weight Heparins (LMWH) or oral anticoagulants). In December 2019, Royal Free Hospital (RFH) developed a guideline for use of low dose tissue plasminogen activator (Alteplase) thrombolysis (l-tPAT) for splanchnic vein thrombosis. This therapy has been used in the treatment of 40 patients between 2014 and 2019 with variable success. The aim of this audit was to investigate if patients are appropriately initiated and monitored on l-tPAT in line with the guideline, clinical and radiological outcomes, and the impact of specialist pharmacist interventions.

Method All patients initiated on l-tPAT for splanchnic vein thrombosis from December 2019 to March 2021 at RFH were investigated. Data from electronic dispensing records, patient notes, prescriptions, and discharge letters were used to determine if patients met initiation criteria, investigate changes made to l-tPAT, response to therapy, patient outcomes and pharmacist interventions.

Results A total of 25 patients received l-tPAT. The mean age was 48 years with a Male:Female ratio of 14:11. 100% of patients met initiation criteria. Treatment was interrupted due to low fibrinogen in 46%(11) and adverse effects( AE) recorded in 29%(7). 8%(2) stopped due to AE with 4%(1) suffering a serious AE. Overall, 58%(14) of patients had therapy interrupted and/or stopped due to blood test abnormalities and/or adverse effects. Figure 1 shows outcomes following imaging review. 56%(14) had identifiable risk factors for thrombosis. Small bowel resection was eventually required in 3 patients. A total of 104 pharmacy interventions were recorded for 20 patients, the majority on appropriate initiation (28%), prescribing (27%) and monitoring (13%).

Conclusion Initiation of l-tPAT was appropriate in all patients. Due to the majority of patients experiencing a decrease in fibrinogen and/or AE, this therapy requires close biochemical and patient monitoring. Specialist pharmacist input is key in ensuring appropriate initiation, prescribing and monitoring and hence, patient safety when on high-risk therapy. Patient outcomes at first review showed that 46% of patients showed no recanalisation of their clot burden with 29% requiring Transjugal intrahepatic portosystemic shunt (TIPSS) ± Catheter Directed Thrombolysis (CDT) and 13% small bowel resection. A larger sample size with evaluation of long-term patient outcomes is required to establish the overall effectiveness of l-tPAT.
Continued analysis of real-world data is important to better establish the natural history of immunotherapy related hepatitis. Lancashire Teaching Hospitals is the tertiary cancer centre for Lancashire and South Cumbria. Electronic records, biochemistry results and oncology prescribing databases were retrospectively analysed for 68 patients treated with Ipi/Nivo between August 2016 and October 2020.

36 (52.9%) patients experienced hepatotoxicity (any grade) with n= 11 (16.2%) patients developing grade 3 or 4 hepatitis. The median time of onset of hepatotoxicity from the first dose (all grades) was 40 days (range 8–322).

Amongst patients who experienced hepatotoxicity, the proportion treated with intravenous, oral or nil corticosteroids was 47.2%, 38.9% and 13.9% respectively. 4 patients required escalation to MMF and 1 patient needed tacrolimus as a third agent. Of patients who developed hepatotoxicity, n=29 had combination treatment discontinued prior to completion of 4 cycles. 15 patients were re-challenged with single agent nivolumab. Of the patients re-challenged, n=9 (60%) did not experience any further hepatotoxicity.

This data demonstrated Ipi/nivo induced hepatitis occurring at a higher rate than in reported studies. This highlights the importance in monitoring real world data with novel anti-cancer therapies however, larger collaborative datasets are required. In addition, further comparative effectiveness research regarding treatment with oral vs intravenous corticosteroids will be important. The latter usually requires hospital admission, which has cost, service and patient experience implications.

Abstract P017 Figure 2

Abstract P017 Figure 3

Summary of overall incidence of immunotherapy related hepatotoxicity according to grade and pattern of liver injury
implications. Finally, further analysis of phenotypic and biochemical variables associated with hepatotoxicity may identify important trends to allow better prediction and thus appropriate counselling and informed discussion when planning treatment.

REFERENCES