

BASL Alpha-1 antitrypsin SIG meeting 17.11.22

Present: Aftab Ala, James Allinson, Andrew Deans, Bill Griffiths, John Hirst, Nick Hopkins, David Parr, Tamir Rashid, John Ryan, Alice Turner, Mike Williams

PiZZ cohort - Tamir Rashid

Assembling national registry:

Currently 1984 homozygotes across sites in England: 89% adults, 53% male.

Future work - integrating EMRs, prospective study (requires £2 million), links with Scotland and Ireland (Mary Bythell, NHS Digital, establishing framework). Appetite to further collaboration - ?aim for NIHR call.

Family screening/primary care referral pathway for Scotland - Andrew Deans, Edinburgh

All alpha-1 phenotyping (IEF) done in one lab therefore makes sense to have a system in place of who to test/who to refer. Proposed pathway details shared with group. Concentrates mainly on ZZ referral to respiratory +/- hepatology with other genotypes depending on liver risk factors/scores.

Discussion - ?refer all 'low levels', SZ may need respiratory review, may be difficult to implement south of the border due to pressures and issues with 'genetic' testing in primary care. It will be interesting to see results of Scottish programme. GP representation on alpha-1 SIG would be helpful - may be more accessible via respiratory route. *Action: if anyone knows a GP already interested please pass on*

Clinical standards for A1ATD - Bill Griffiths

Document shared with group – recognized this has been drawn up by a hepatologist so would benefit from further respiratory input. Could be some merit in joined up working between hepatology and respiratory for UK/Ireland standards given now several combined services and new treatments on the horizon. From liver side, recognition that 30% of adults develop significant fibrosis and that we now have tools to monitor (fibroscan) - emphasis will mainly be on liver risk reduction until new therapy online. Lung management is that of COPD essentially.

Some guidelines are out there - European Taskforce paper not done via guideline methodology and US not interested (Alice Turner). Recent EARCO discussion - likely ERS guideline route. There are DELPHIs in progress which could wait for - I do not think there is a liver one yet having spoken to Pavel Strnad (liver ERF) about this at EASL in June. Questions raised about whether it is possible to combine a liver and respiratory guideline though we did a similar venture in Wilson's disease recently (liver/neuro - Lancet Gastro Hep Apr 22). There is unmet need in terms of variation in care and timely diagnosis. Advice to general hepatologists/respiratory physicians via guidance of some description could be helpful. The patient groups are likely to be keen. *Action: BG to flesh out some ideas of what would be helpful to 'jobbing clinicians' (contributions welcome from the group).*

Clinical trials - Bill Griffiths

Main focus from liver side is siRNA therapy - recent NEJM publication on fazirsiran (Arrowhead/Takeda), Novo nordisk (Dicerna)'s Estrella study recruiting in Cambridge (+ now Leeds?). Vertex pursuing protein inhibitors on liver side - VX-864 and VX-634 (2nd gen). Gene editing further away. Inhbrx study on recombinant alpha-1 (several UK centres). Neutrophil elastase inhibitors in development. Tamir mentioned the sizeable problem of MZ exacerbating NAFLD and now looking amenable to pharma intervention.

Next meeting TBA