PREDICTING RESPONSE TO TREATMENT

In a satellite symposium sponsored by Janssen Pharmaceuticals, Dr Bram Verstockt, Belgium, talked about the ongoing search for biomarkers that can predict response to treatment for IBD.

Dr Verstockt began by presenting a case. It was a 50 year old woman with Crohn's disease (CD), who was treated with azathioprine.

Many ways of profiling

– In 2010, she had a resection of colon transversum due to symptomatic structure. In 2014 she had a flare with active colitis, and was treated with adalimumab. In 2015, adalimumab was discontinued due to adverse events and in 2016 after a flare with active colitis she was treated with vedolizumab.

He told the audience that after 6 months of adalimumab she had a SES-CD (Simple endoscopic score in CD) of 18. Finally she was treated with ustekinumab – and after 6 months her SES-CD score was 0.

– Could we have *predicted* her disease course – her response to biological agents and her anti-TNF reported adverse events?

There are many ways for profiling an IBD-patient – with genetics, transcriptomics, metabolomics and proteomics among others.

– But very little of this can give us predictive values for the clinic. So there is still a lot of work to do, Dr Verstockt said.

The targets are moving

The PROFILE trial in CD is on finding a molecular surrogate marker in blood that can differentiate patients into expected benign and severe disease courses.

All participants, after biomarker assessment, receive established treatments and are randomly allocated to two groups. One group is receiving top-down treatment, and the other group standard step-up treatment.

The aim of the study is to see if there is a biomarker that allows for choosing the right strategy for the right patient at diagnosis.

The trial is ongoing.

– In general CD care, what we currently are doing is to apply the "one size fits all" strategy to our patients. This leads to both over- and under-treatment. In the future I think we might be able to predict response to a specific therapy, Dr Verstockt envisioned.

The next question is to determine *which* therapy to use – and this is even more challenging to do.

– We should treat to target, but the targets are moving – symptoms and quality of life, endoscopy, biomarkers and histology can all constitute a target. Another point is to also take pharmacokinetics and pharmacodynamics in consideration, he pointed out.

To early to use predictive biomarkers in the clinic

When it comes to predicting response to anti-TNF, genetics is one way to go.

– Another way is to take metabolomics/metagenomics in consideration when searching for a biomarker, Dr Verstockt said.

In anti-TNF non-responders, TNF-driven pathways are significantly upregulated. Also TNF messenger-RNA is significantly upregulated.

– Higher doses of anti-TNF might work for some of these patients, he commented.

At present, there are very little data on anti-IL12 molecules.

– It is too early to start using predictive biomarkers in the clinic, Dr Verstockt summarised.

However, the future looks bright – but challenging, he added.

– We need replication of identified biomarkers, tested in clinical trials. We also need consensus about the desired outcome and definition of response.

There is a need for bioinformatics enabling integration of multi-omic datasets.

– Finally, we need to increase power by merging big cohorts, academia and industry.

Dr Verstockt finished his talk by presenting COLLIBRI – which stands for the collaborative IBD biomarker research initiative.

Per Lundblad