Review of the 63rd American Society of Haematology Annual Meeting and Exposition

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I am grateful to have received a UKMF/GSK joint bursary to allow me to attend the 63rd ASH meeting in Atlanta, Georgia. This was my first-time attending ASH and it did not disappoint. I was given the opportunity to present my PhD research as a poster titled 'TRIM33 Loss in Multiple Myeloma Impairs the DNA Damage Response Resulting in Sensitivity to PARP and ATR Inhibitors' and enjoyed being able to discuss it with other scientists and receive positive feedback.

ASH did a great job of ensuring the safety of in-person participants, with COVID-19 testing facilities available at both the congress centre and nearby hotels, mask and vaccination requirement and endless sanitiser. Moreover, the immense size of the centre always allowed for social distancing. For those unable to attend in-person ASH provided an excellent online platform for virtual attendance, which also proved useful for catching up on missed sessions since it became clear that there was simply too much to squeeze in to 4 days!

I attended mainly scientific sessions as these were most relevant to my background. Of interest was a talk by Sarah Gooding, University of Oxford, who presented data on copy number alterations that can drive IMiD resistance in MM. Based on CRISPR/Cas9 and shRNA-based screens, this group identified that loss of chromosome 2q containing *COPS7B* and *COPS8* may drive resistance to lenalidomide and pomalidomide as it becomes clonal during treatment. This highlights that there may be other factors contributing to IMiD resistance other than CRBN regulation. Paula Restrepo, Icahn School of Medicine at Mount Sinai, gave a great presentation on the identification of a 3-gene signature that can predict response to Selinexor. Selinexor is a recently approved therapy for MM that works by inhibiting the nuclear export protein XPO1. Analysis of RNA-Seq data revealed 3 genes – WNT10A, DUSP1 and ETV7 that are upregulated in patients who respond to Selinexor and have improved PFS following treatment. This was validated in vitro whereby siRNA knockdown of all 3 genes was required for resistance to Selinexor. Moreover, this gene signature was shown to be specific to Selinexor response and may be a promising approach to aid treatment selection in the future.

Eileen Boyle, Perlmutter Cancer Center, NYU Langone Health, presented interesting data on genomic and immune signatures that may predict sustained MRD negativity in daratumumab-based combination therapy. In this study, not only were CD38+ tumour cells sequenced, but additionally the bone marrow cellular content was sequenced to provide information on the immune microenvironment. Failure to achieve sustained MRD negativity was associated with del(13q), del(22q)/delXBP1

and 8q gains. Additionally, analysis showed that delXBP1 was associated with fewer memory B-cells, naïve B-cells, and dendritic cells indicating that the immune microenvironment may also drive response.

Numerous talks and posters were also presented from the iStopMM study which aims to screen adults in Iceland for the earliest signs of MM. Data showed that 0.5% of the general population have smouldering MM. A hot topic was that the iStopMM study reported no association between MM pre-cursor MGUS and severity of COVID-19 disease or susceptibility to infection which is contrary to various reports that MM is associated with increased COVID-19 severity. As expected, discussions of MGUS and smouldering MM lead to debates on when is appropriate to begin treatment, with many studies aiming to risk-stratify these pre-cursor states.

Overall, I found the ASH experience extremely informative and a great opportunity to learn about the top novel science in the field of myeloma and meet some excellent scientists. I again thank the UKMF and GSK for supporting my attendance to such a significant event.