Report on International Myeloma Society (IMS) Annual Meeting 2025

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Firstly, I would like to extend my heartfelt thanks for the support from the UK Myeloma Society (UKMS)-Sanofi joint bursary, which allowed me to attend and present my research at the IMS Annual Meeting 2025, held in Toronto, Canada, from 17-20 September. The conference served as a global platform bringing together clinicians, researchers, and industry experts dedicated to advancing multiple myeloma research and patient care. As one of the most important gatherings in the field of myeloma, the meeting showcased cutting-edge developments spanning basic, preclinical, and clinical research, with a strong emphasis on translating novel discoveries into improved therapeutic strategies. The program was structured around four thematic areas: Precursor Disease, Risk Adaptation Management, Immunotherapy, and Relapse within 1-3 Lines of Therapy; reflecting the field's rapidly evolving priorities and translational focus.

In general, there was an increasing emphasis on immunotherapy, as a cornerstone of current and future myeloma treatment. Prof. Tak Mak's keynote lecture provided an overview of the role of γδ T-cells in the anti-myeloma response to antibody-drug conjugates (ADC), in the ALGONQUIN trial. Expansion of these cells correlates with therapeutic response and that their unique HLA-independent recognition profile could pave the way for "off-the-shelf" TCR-based immunotherapies. Also, early results from the DREAMM-20 trial (presented by Hang Quach), which evaluated an unconjugated form of Belantamab for relapsed/refractory multiple myeloma, showed robust anti-myeloma activity with an excellent safety profile and minimal ocular toxicity compared to the conjugated Belantamab mafodotin. The TRIgnite-1 study introduced a tri-specific antibody (BCMAxCD38xCD3) with promising early data, while HDP-101, an anti-BCMA ADC with a novel amanitin payload, demonstrated notable activity and tolerability in heavily pretreated patients. On a broader level, the clinical data collectively signalled that bi- and tri-specific T-cell engagers are moving to earlier treatment lines, building upon the success of CAR-T therapy, and that ADCs continue to evolve with optimised dosing schedules and improved safety profiles.

Complementary sessions offered valuable biological context to these clinical advances. The complex immune landscape in extramedullary myeloma, revealed reduced cytotoxicity among $CD8^+$ T cells and an enrichment of $CD16^-$ NK cells which are findings that may inform future immunotherapeutic strategies (presented by Anjana Anilkumar Sithara). The pooled European pooled analysis involving a large cohort of 2432 patients presented by Bertamini demonstrated the clinical utility of circulating tumour cells (CTCs) in improving risk stratification for newly diagnosed myeloma and plasma cell leukaemia patients. Together, these studies reflected a shift toward integrating immune profiling and spatial biology to guide therapeutic decision-making. Among the other therapeutic approaches are the encouraging clinical data on Cemsidomide, a next generation cereblon E3 ligase modulator, which showed durable activity and favourable tolerability in combination with dexamethasone with a potential for combination regimens in relapsed/refractory settings.

The sessions on precursor disease states collectively emphasised that transformation from precursor stages to overt malignancy is not always a linear process. Studies presented by Kim and Ghobrial highlighted the concept of *Monoclonal Gammopathy of Indeterminate Potential (MGIP)* as an even earlier detectable premalignant stage that can potentially progress to plasma cell and B-cell malignancies with significant implications on risk stratification, early detection and patient monitoring. Complementing these, Samur's analysis of paired smouldering and myeloma samples revealed that many patients already harbour malignant subclones at diagnosis, underscoring the need to redefine existing clinical categories. Collectively, these talks reflected a growing consensus that early detection and refined risk stratification will be central to preventing disease progression.

From a personal perspective, attending IMS 2025 provided an invaluable opportunity to connect my own research with these emerging developments. I presented a poster titled "*Anti-adhesion Properties of KTX-1001, a Selective NSD2/MMSET Inhibitor, Enhance Carfilzomib Sensitivity in Multiple Myeloma*," which explored how targeting NSD2 disrupts adhesive interactions and sensitises drug-resistant cells to proteasome inhibitors. The discussions and feedback I received helped refine my experimental direction and reinforced the importance of integrating epigenetic targeting with immunotherapy-based approaches.

Overall, attending the IMS Annual Meeting 2025 in Toronto was an immensely enriching experience that provided an outstanding opportunity to engage with leading experts and emerging research in multiple myeloma. The conference experience was deeply motivating, offering new perspectives on my work and strengthening my resolve to contribute to the evolving field of myeloma research. The insights gained, both from scientific discussions and informal interactions, will undoubtedly guide my future studies and foster collaborations aimed at improving patient outcomes.