Background

- Newly diagnosed High Risk Myeloma and primary Plasma Cell Leukemia (PCL) have a high unmet need and novel approaches for these groups are urgently needed.
- Standard therapies lead to very short PFS and OS in patients with molecular High Risk MM, specifically:
  - Double-hit tumors (any 2 of t(14;16), t(14;20), del(17p))
  - GEP High Risk signature tumors, such as SKY92
- We designed and conducted a prospective, multi-center risk-stratified trial for NDMM High Risk and PCL patients, using an innovative and novel treatment approach.

Design

- The OPTIMUM MUK9 trial consists of the central OPTIMUMscreen protocol (MUK9A) and the OPTIMUMtreat protocol (MUK9B) offered to patients found to have High Risk MM on central results (Figure 1).
- Central molecular profiling of CD138-selected tumour material consisted of IGH translocation (RT-qPCR), copy number aberration (CNA) (MLPA; MRC Holland) and GEP SKY92 risk profiling (MMPoller; SkylineDiAGenetics). A maximum of 2 cycles of VTD standard of care induction could be given whilst central results were pending. Patients with newly diagnosed primary PCL were offered direct enrolment into MUK9B.
- OPTIMUMtreat MUK9B therapy consisted of daratumumab, cyclophosphamide, bortezomib-augmented single HD-MEL+, and lenalidomide, dexamethasone induction (Dara-CV Rd consolidation 1, Dara-VRd consolidation 2 and Dara-R)
- Patients could receive VTD SOC whilst central BM results were generated, none progressed during this phase.
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- OPTIMUM is one of the first trials to prospectively enrol PCL in the era of modern therapies (Table 1).

Conclusions

- OPTIMUM demonstrates feasibility of centrally stratified Risk Adapted therapy.
- This is enabled by availability of modern therapies (T cell engagement) for patients and physicians/care teams.
- Colleagues: We are grateful for support from Janssen and Celgene; we acknowledge support by MyelomaUK during initial trial planning. MK is supported through a Jacob’s Trust Foundation Fellowship.


Results

- OPTIMUM recruited between Sept 2017 – July 2019 when it reached recruitment target of 108 High Risk/PCL OPTIMUMtreat patients (Figures 1&2).
- Recruitment speed accelerated throughout the trial and completion 9 months ahead of projections. Star = Recruitment speed accelerated throughout the trial and completion 9 months ahead of projections. Star =