Clonotypic Peptide Mass Spectrometry to Define Functional Cure in Patients with Multiple Myeloma Undergoing Maintenance Cessation

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BACKGROUND

- Mass spectrometry (MS) can achieve lower levels of detection of myeloma M-protein vs serum immunofixation (IFIX), especially using the **clonotypic peptide approach.**
  - –Limit of detection is **1000x** more sensitive than IFIX
- M-InSight (Sebia/Corgenix) is a clonotypic peptide assay that involves M-protein *de novo* sequencing and peptide quantification to accomplish highly sensitive blood-based monitoring of the M-protein.
- **We assessed clonotypic peptide MS status using M-InSight among patients on the MRD2STOP study.**

- **Trace M-proteins were still detectable** in the blood by clonotypic peptide MS despite MRD < 10^{-6} and MRD <10^{-7}
- **Disease resurgence** among patients who discontinued maintenance may be predicted by a **log-fold increase in M-protein concentration.**
- **Clonotypic peptide MS may serve as a key marker for cure in MM.**

Figure 1: Baseline M-Protein Concentration

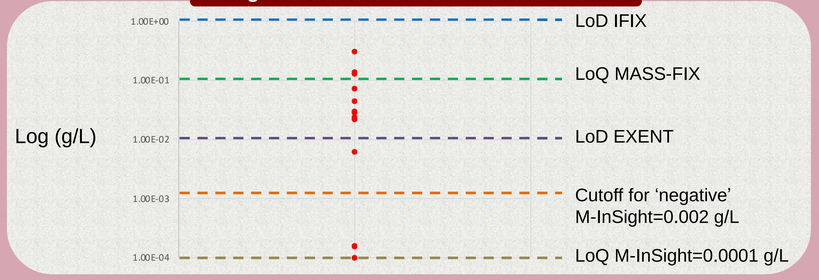
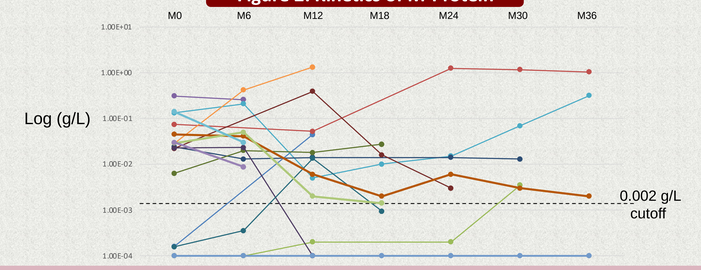
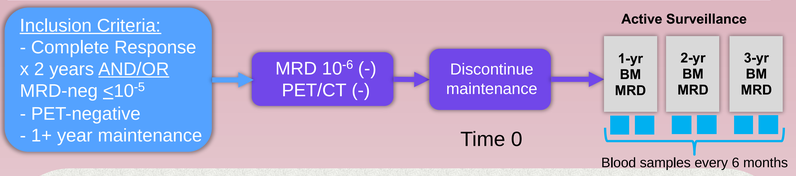


Figure 2: Kinetics of M-Protein



- M-protein concentration increased in 8/16 (50%) pts
- 6 pts w/disease re-emergence: 2 w/MRD 10^{-6} resurgence (dotted) & 2 w/ progression (solid)
- Disease re-emergence was pre-empted by a log-fold increase in M-protein in 5/6 (83%) patients; only 3/10 (30%) with sustained MRD(-) had a logfold increase

METHODS



- High-disease burden baseline patient serum samples were required (M-spike ≥ 0.2 g/dL or FLC ≥ 40 mg/dL)
- Baseline samples were digested with several combinations of proteolytic enzymes to permit sequencing of the M-protein heavy & light chain.
- Clonotypic peptides specific to the patient's CDR were selected for MS quantification using a bioinformatics algorithm & compared to RNA sequencing data.

RESULTS

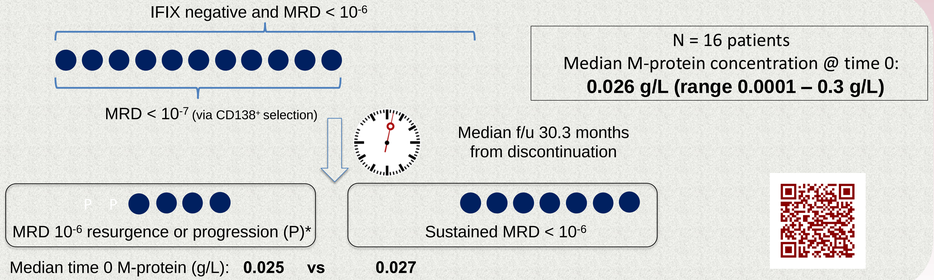
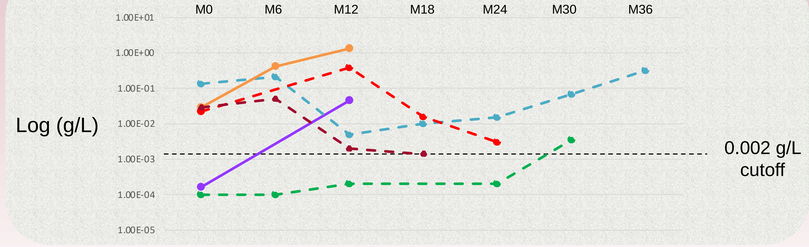


Figure 3: Kinetics of M-Protein in Patients with Disease Re-Emergence



Of the first 11 patients samples, 10 (91%) had sequence homology between the M-InSight-derived M-protein sequences and the clonoSEQ-derived sequences.