t(11;14) status is stable between diagnosis and relapse and concordant between detection methodologies based on fluorescence *in situ* hybridization and next-generation sequencing in patients with multiple myeloma

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Supplemental Information

Supplemental Methods

Statistical Power Calculation

Power calculation was based on the samples needed for the primary objective (stability of t(11;14) status between diagnosis and relapse). With an assumed prevalence of t(11;14) positivity at 15% in patients with MM, and the observed stability rate of 91% between samples at diagnosis and relapse (equivalent to a Kappa of 0.65), 182 bone marrow samples from patients with MM were needed to have ≥80% power to observe a significantly better Kappa than 0.4 with type I error at 0.025 one sided. Allowing for a technical failure rate at 10%, longitudinally paired samples would need to be collected from 200 patients to allow for 182 pairs of evaluable samples.

Bioinformatics Pipeline

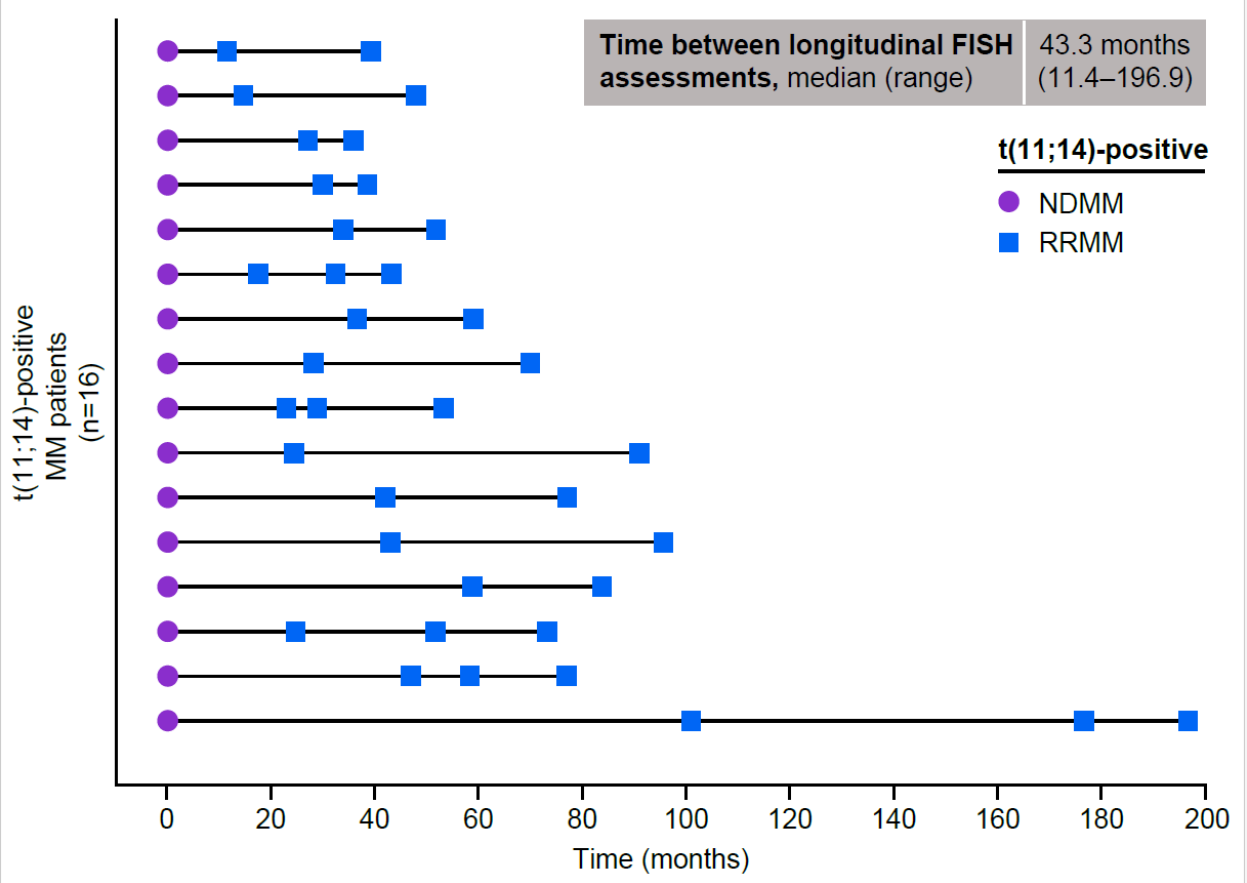
Raw sequencing data were processed by an in-house bioinformatics pipeline to detect mutations, copy number aberrations (CNAs), and structural variants (SVs). Protein coding mutations with variant allele frequency >10% and minimum sequencing depth >=20X were selected. CNAs were defined as log ratio above 0.3 (copy number gain) or below –0.4 (copy number loss). SVs with 5 or more supporting reads were examined to detect translocations within the *IGH* locus.

Statistical Method

t(11;14) status (positive vs negative) determined by FISH in bone marrow samples at diagnosis was tabulated against t(11;14) status in bone marrow samples at relapse. Stability of t(11;14) status between samples collected at initial diagnosis and first relapse was assessed by determining the percentage of patients whose t(11;14) status was the same in the samples collected at diagnosis and at relapse. The concordance of t(11;14) status between FISH and NGS was assessed by determining the percentage of patient samples for which t(11;14) status results of these 2 tests were in agreement. 95% CIs were also calculated. Statistical significance was defined as $P<0.05$.

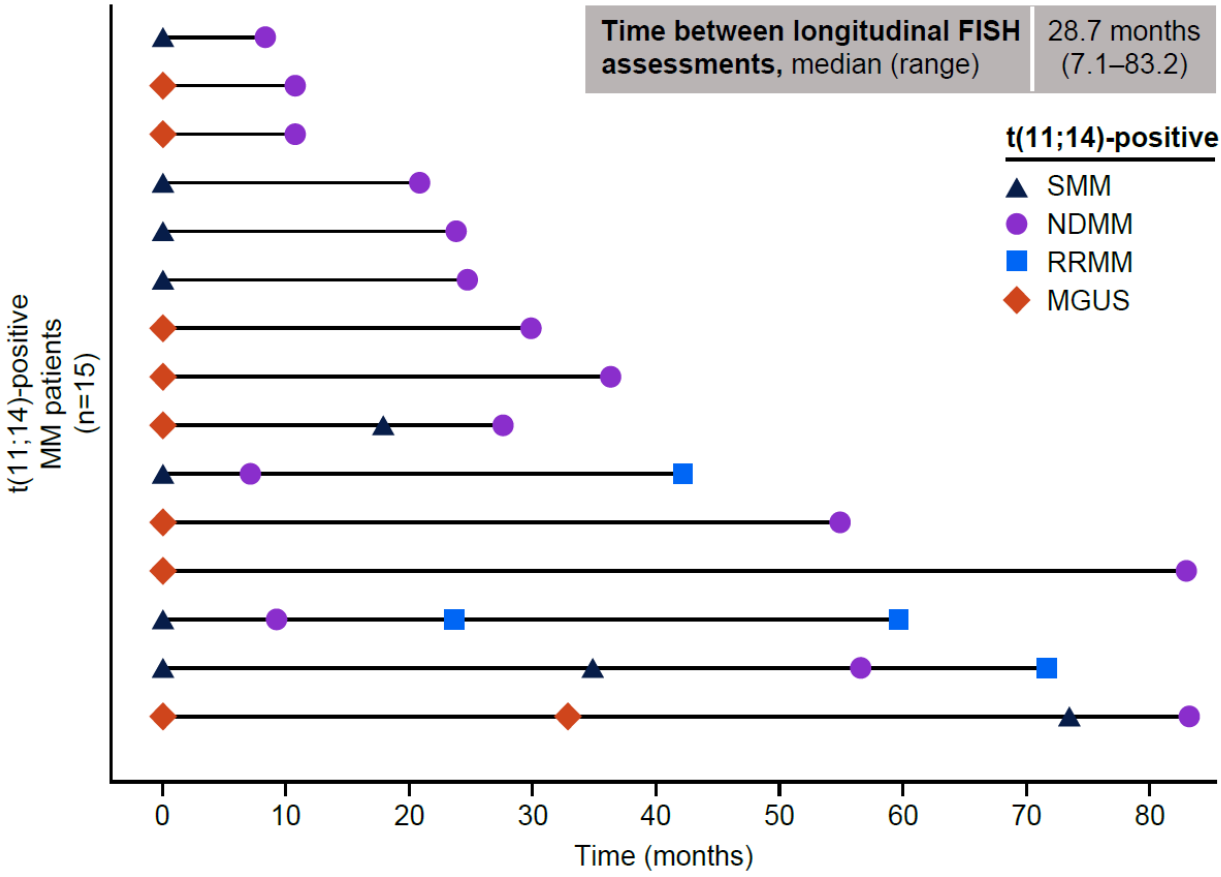
Supplemental Figures

Supplemental Figure 1. FISH Assessments of t(11;14) Alterations at Diagnosis and Through Multiple Rounds of Relapse



NDMM, newly diagnosed multiple myeloma; RRMM, relapsed refractory multiple myeloma

Supplemental Figure 2. FISH Assessments of t(11;14) from Initial Detection in MGUS/SMM to Diagnosis and Progression of NDMM



MGUS, monoclonal gammopathy of undetermined significance; NDMM, newly diagnosed multiple myeloma; RRMM, relapsed refractory multiple myeloma; SMM, smoldering multiple myeloma