Telomere dynamics in patients with del (5q) MDS before and under treatment with lenalidomide

Myelodysplastic syndrome (MDS) associated with an acquired, isolated deletion of chromosome 5q (del (5q) MDS), represent a clonal disorder of hematopoiesis and a clinically distinct entity of MDS. Treatment of del (5q) MDS with the drug lenalidomide has significantly improved quality of life leading to transfusion independence and complete cytogenetic response rates (CCR) in the majority of patients. Telomeres are located at the end of eukaryotic chromosomes and are linked to replicative history/potential as well as genetic (in) stability of hematopoietic stem cells. Here, we analyzed telomere length (TL) dynamics before and under lenalidomide treatment in the peripheral blood and/or bone marrow of del (5q) patients enrolled in the LEMON-5 study (NCT01081431). Hematopoietic cells from del (5q) MDS patients were characterized by significantly shortened TL compared to age-matched healthy controls. Telomere loss was more accelerated in patients with longer disease duration (> 2 years) and more pronounced cytopenias. Sequential analysis under lenalidomide treatment revealed that previously shortened TL in peripheral blood cells was significantly \"elongated\" towards
normal levels within the first six months suggesting a shift from clonal del (5q) cells towards normal hematopoiesis in lenalidomide treated MDS patients. Taken together our findings suggest that the development of the del (5q) clone is associated with accelerated telomere shortening at diagnosis. However, upon induction of CCR and reoccurrence of normal hematopoiesis, the lack of a persistent TL deficit argues against telomere-mediated genetic instability neither as a disease-promoting event of del (5q) MDS nor for lenalidomide mediated development of secondary primary malignancies of the hematopoietic system in responding patients. (C) 2015 Elsevier Ltd. All rights reserved.