RESEARCH FOR RARE
Forschung für seltene Erkrankungen

Paper of the Quarter – QI/2024 – MyPred

Spontaneous remission and loss of monosomy 7: a window of opportunity for young children with SAMD9L syndrome

Haematologica. 2024 Feb 1. *>>PubMed-Link<<*

Miriam Erlacher, Felicia Andresen, Martina Sukova, Jan Stary, Barbara De Moerloose, Jutte van der Werff Ten Bosch, Michael Dworzak, Markus G Seidel, Sophia Polychronopoulou, Rita Beier, Christian P Kratz, Michaela Nathrath, Michael C Frühwald, Gudrun Göhring, Anke K Bergmann, Christina Mayerhofer, Dirk Lebrecht, Senthilkumar Ramamoorthy, Ayami Yoshimi, Brigitte Strahm, Marcin W Wlodarski, Charlotte M Niemeyer

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Für manche Patient:innen, die auf Grund einer genetischen Veranlagung eine myeloische Neoplasie entwickeln, bleibt eine hämatopoetische Stammzelltransplantation mit all ihren Risiken die einzige Chance auf Heilung. Insbesondere bei Verlust eines der beiden Chromosomen 7 (Monosomie 7) gibt es meist keine therapeutischen Alternativen.

Mehrere MyPred-Partner berichten in der Fachzeitschrift Haematologica von Patient:innen, die trotz Monosomie 7 keine Transplantation benötigt haben. Es handelt sich dabei um junge Kinder (<5 Jahre) mit einem sogenannten SAMD9L-Syndrom, also mit einer angeborenen SAMD9L Mutation. Bei diesen Kindern kann eine spontane Verbesserung von Knochenmarkfunktion und Blutbild auftreten. Auch die Monosomie 7 und das damit verbundene Leukämierisiko können wieder verschwinden. Die Autoren diskutieren basierend auf diesen Fallbeispielen die Vorteile, Risiken und Voraussetzungen für eine mögliche „watch-and-wait“ Strategie.

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Monosomy 7 is the most common cytogenetic abnormality in pediatric myelodysplastic syndrome (MDS) and associated with a high risk of disease progression. However, in young children, spontaneous loss of monosomy 7 with concomitant hematologic recovery has been described, especially in the presence of germline mutations in SAMD9 and SAMD9L genes. Here, we report on our experience of close surveillance instead of upfront hematopoietic stem cell transplantation (HSCT) in seven patients diagnosed with SAMD9L syndrome and monosomy 7 at a median age of 0.6 years (range, 0.4-2.9). Within 14 months from diagnosis, three children experienced spontaneous hematological remission accompanied by a decrease in monosomy 7 clone size. Subclones with somatic SAMD9L mutations in cis were identified in five patients, three of whom attained hematological remission. Two patients acquired RUNX1 and EZH2 mutations during the observation period, of whom one progressed to myelodysplastic syndrome with excess of blasts (MDS-EB). Four patients underwent allogeneic HSCT at a median time of 26 months (range, 14-40) from diagnosis for MDSEB, necrotizing granulomatous lymphadenitis, persistent monosomy 7, and severe neutropenia. At last follow-up, six patients were alive, while one passed away due to transplant-related causes. These data confirm previous observations that monosomy 7 can be transient in young children with SAMD9L syndrome. However, they also indicate that delaying HSCT poses a substantial risk of severe infection and disease progression. Finally, surveillance of patients with SAMD9L syndrome and monosomy 7 is critical to define the evolving genetic landscape and to determine the appropriate timing of HSCT (clinicaltrials gov. Identifier: NCT00662090).

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