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Introduction:
Moderately-effective therapies (MET) have been the main treatment in pediatric-onset multiple sclerosis (POMS) for years. Despite the expanding use of highly-effective therapies (HET), therapeutic guidelines for POMS are missing.

Objectives/Aims:
To assess the real-world effectiveness of HET as immediate treatment compared with MET on disease activity.

Methods:
In this retrospective observational study, we used data from 36 French MS expert centers participating in the Observatoire Français de la Sclérose en plaques (OFSEP), the French MS registry. We included treatment-naïve children (aged under 18 years) with relapsing-remitting MS who initiated HET or MET from 2010 to 2022. We used an innovative statistical method to model the logarithm of event rates by a penalized splines of time, allowing the possibility to model the effects of covariates in a flexible way considering non-linearity and interactions.

Results:
A total of 530 children were identified and met inclusion criteria (422 MET and 108 HET). Both HET and MET treatment strategies reduced the risk of first relapse within the first 2 years. HET dampened the occurrence of a first relapse with a 54% risk reduction compared to MET (adjusted Hazard Ratio HR 0.46 [95% CI 0.31-0.67]; p<0.001) and a sustained effect over 5 years of follow-up, confirmed on MRI activity (adjusted OR 0.34 [95% CI 0.18-0.66]; p=0.001) and with a better tolerability pattern. MET had six times more risk of discontinuation at 2 years (HR 5.97 [95% CI 2.92-12.20]). Index treatment was not associated with enrollment in tertiary education.

Conclusion:
HET as first-line strategy in POMS reduces the occurrence of a first-relapse with an optimal effect within the two first-years compared to treatment escalation, supporting a need to use immediate HET in POMS.

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