

## ODISSEY: A MULTICENTER, OBSERVATIONAL STUDY OF MULTIPLE MYELOMA PATIENTS WHO DISCONTINUED THERAPY IN CLINICAL PRACTICE

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**Introduction:** Nowadays continuous treatment until disease progression or unacceptable toxicity remains the main approach in multiple myeloma (MM). However, prolonged exposure may lead to cumulative toxicity, treatment fatigue and quality-of-life impairment. In clinical practice, a not negligible number of patients discontinues therapy due to medical, personal, or logistic reasons. Recent evidence from time-limited regimens has renewed interest in whether discontinuation may be feasible and safe in selected cases. **Methods.** The ongoing ODISSEY study (A multicenter, Observational study of multiple myeloma patients who discontinued therapy in clinical practice) was designed to describe clinical features and outcome of MM patients who discontinued treatment for reasons other than disease progression or death and were alive in remission for at least 12 months, aiming to identify predictors of prolonged treatment-free remission (TFR). **Results.** Fifty-one patients diagnosed between 2007 and 2022 have been so far enrolled. The median age at discontinuation was 73 years (range, 52-88). At diagnosis, eighteen patients (35.3%) were in ISS stage I; seventeen (33.3%), in stage II; sixteen (31.4%), in stage III. Treatment was discontinued during first, second and third or subsequent lines in 25 (49.1%), 22 (43.1%) and 4 (7.8%) patients, respectively. Specifically, discontinuation in first line mainly occurred during lenalidomide/thalidomide maintenance (52%) and in second line

mainly under daratumumab/carfilzomib-lenalidomide-dexamethasone combinations (63.6%). The median duration of treatment leading to discontinuation was 23 months (range, 2-87), overlapping the median treatment duration from best-response achievement to discontinuation. At suspension of therapy, most of patients (80.4%) were in complete response (34 CR; 7 sCR). Main reasons for discontinuation were non-hematologic toxicity (25.6%), shared medical decision (19.6%), hematologic toxicity (15.7%), patient's choice (11.7%), newly acquired comorbidities (11.7%), or other causes (15.7%). Median TFR was 46 months (95%CI 41-NR) (Figure 1). At a median follow-up of 26 months (range, 9-130) from treatment discontinuation, 44 (86.3%) patients were alive and most of them (84.1%) were still in remission. **Conclusions.** The ODISSEY study represents one of the first real-world experiences exploring treatment discontinuation in MM outside of clinical trials. Despite heterogeneous therapeutic settings, a subset of patients achieved durable off-therapy remissions, supporting the feasibility of treatment cessation in selected cases. Future studies incorporating measurable residual disease assessment could validate these preliminary findings. In a broader perspective, ODISSEY contributes to the concept of sustainable MM care, integrating efficacy, safety, quality of life, and optimization of healthcare resources, with reduced drug exposure, lower treatment-related costs, and fewer hospital visits.

MONOCLONAL GAMMOPATHIES & MULTIPLE MYELOMA

