Background MSI-H derives from genomic hypermutability due to deficient mismatch repair (dMMR) function. dMMR can occur for epigenetic silencing or mutations in MMR genes, whose germline alteration cause Lynch syndrome (LS). Colorectal (CRC) and endometrial cancers (EC) more often have MSI-H, but various tumors can present this molecular feature. Immunotherapy demonstrated high efficacy in MSI-H advanced cancer, and pembrolizumab and dostarlimab gained anagnostic approval for these patients by FDA.

Methods We retrospectively reviewed the records of patients that started a treatment in the Phase I Unit of the European Institute of Oncology between January 1st 2014 and June 15th 2023 to identify patients with MSI-H/dMMR tumors. We performed descriptive statistics and survival analysis. The study was approved by European Institute of Oncology Ethical Committee (Number UID 3560).

Results We identified 17 MSI-H patients enrolled in a phase I trial at our institution (table 1). The median age was 67.0 years (range 49–76); 11 were female and 6 male. Most frequent cancer types were CRC (6), and EC (4). The mean number of previous lines was 1.5. See table 1 for baseline characteristics of patients. All patients received various anti-PD1 monoclonal antibody (MAB) in clinical trials, 16 as monotherapy and 1 in combination with anti-LAG3 MAB + adenosine A2A receptor antagonist. Two patients had complete response, 9 patients had partial response (PR) and 1 had stable disease, with an objective response rate of 64.7% (figure 1). After a median follow-up of 38.8 months (R 0.2–70.7 months), 11 patients (64.7%) were alive and 7 (41.2%) did not experience disease progression. Median OS was not reached, and median PFS was 36.2 months. Three patients were affected by LS, 5 had sporadic MSI-H cancer and 9 were not tested for germline mutations. All patients with LS had still ongoing PR (mean 43.5 months). OS and PFS did not differ significantly (p-value 0.19 and 0.07, respectively) between patients with LS and the others (figure 2). Seven patients had at least one immune-related adverse event (irAE). Three patients discontinued the treatment due to G3 irAEs: rash (1 patient), pneumonitis (1) and myasthenia-like syndrome (1).

Conclusions Our analysis confirms the efficacy and the safety of anti-PD-(L)1 MABs in LS patients without signs of reduced efficacy when compared to patients with sporadic MSI-H tumors.
Abstract 530 Figure 1

Abstract 530 Figure 2

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