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TITLE: CAN WAIT AND SEE BE THE STANDARD OF CARE FOR INITIAL APPROACH TO PRIMARY SPORADIC DESMOID TUMORS? PRELIMINARY DATA FROM AN ITALIAN SARCOMA GROUP PROSPECTIVE STUDY.

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ABSTRACT BODY:

Objective: In recent years, retrospective evidence of long term disease stabilization and spontaneous regression of sporadic desmoid tumor (SDT) has been provided. As a result, a frontline wait and see approach (W&S) has been more routinely proposed. CTNNB1 coding for β-catenin is mutated in more than 90% of patients. Furthermore, a specific mutation (45F) was found to be correlated with a worse post-surgical local outcome. However, the prognostic role of β-catenin mutations is not fully understood and has never been explored in patients under W&S before any active therapy is performed. The main objective of this study was to prospectively evaluate the role of W&S in patients with primary SDT and to correlate β-catenin mutational status with the clinical outcome.

Methods: This is a prospective, multicenter (Fondazione IRCCS Istituto Tumori Milano and IRCCS Istituto Candiolo) observational study (founded by Ministero della Salute, Ricerca Finalizzata- NCT 02547831), performed among Italian Sarcoma Group centers and aim at evaluating the progression rate in patients affected by primary SDT managed with a front-line conservative approach (W&S). Active treatments were only proposed upon clear disease progression. βcatenin mutational status has been analyzed.
Inclusion criteria were:
-Pathological diagnosis of SDT
-Primary disease at diagnosis or incompletely resected residual disease (R2 resection)
-Intra- and extra-abdominal SDT
-Histological diagnosis confirmed by expert sarcoma pathologists (PC and MB) according to the WHO criteria
-Measurable disease evaluated by on contrast-enhanced MRI (ce-MRI) T1 and T2 weighted images or contrast enhanced CT scan (for intra-abdominal location) Patient and tumor-related factors, treatment variables, follow up findings, time to progression and status at last followup were recorded.
Follow-up (FU) schedule required clinical evaluation and ce-MRI (or CT scan) at 3, 6, 9, 12 months, then every 6 months until the third year. Upon progression, defined as tumor growth proven by imaging and/or clinical examination, active treatments were proposed according to physician's preference and registered in the clinical database.

Results: Between 2013 and 2018 a total of 114 patients entered the study (82% female, 18% male); median age 39 (IQ, 35-49) years; sites distribution: abdominal wall (52%), trunk (24%), extremity (18%), intra-abdominal (3%), head/neck (3%). CTNNB1 mutational status was available in 87% of patients. Median follow-up was 11 (IQ, 6-23) months. At the time of last follow up: 4/114 had spontaneous

complete regression, 23/114 spontaneous partial regression, 36/114 stable disease, 48/114 progression. For the last 3 patients enrolled status is still unknown. Among patients with stable disease, 6/36 initially experienced a progression and 5/36 initially experienced partial regression, while disease remained stable after that. Among patients with progression, 34/48 needed to start an active treatment. The median time to an active treatment was 6 (IQ range, 4-13) months. A preliminary analysis on the correlation between β-catenin mutational status and outcome revealed that 6/11, 12/51, 4/20 and 5/18 patients with DT harboring 45F, 41A, WT or other mutations had to start an active treatment for progression, respectively. No patient required surgery after enrolment.

Conclusion: This study prospectively confirmed that W&S for primary SDT is safe in light of the high rate of regressions and spontaneous growth arrest. SDT have a favourable course in more than 50% of patients. A higher risk of worse outcome for patients harbouring 45F was observed on the initial analysis but needs further validation on a longer FU. Upon progression, active treatments were considered on an individualized basis, while persisting in the W&S could still pay off.